PHOTOALDRIN AND ITS TOXICITY TO MOSQUITO LARVAE

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In recent years considerable attention has been given to determining more fully the metabolism of insecticides and their fate in the environment. In the case of aldrin (HHDN, I) [2] and dieldrin (HEOD, II) [2] it is now known that these compounds undergo various reactions as shown in Figure 1, including (1) the epoxidation of aldrin to dieldrin in the soil (Gannon and Bigger, 1958), plants (Lichtenstein and Schulz, 1960), vertebrates (Bann, DeCinco, Earle and Sun, 1956), microorganisms and mosquito larvae (Korte, Ludwig and Vogel, 1962); (2) the metabolism of aldrin and dieldrin to *trans*-aldrin-diol in the rabbit (Korte and Arent, 1965) and of dieldrin to Klein's metabolite in the rat

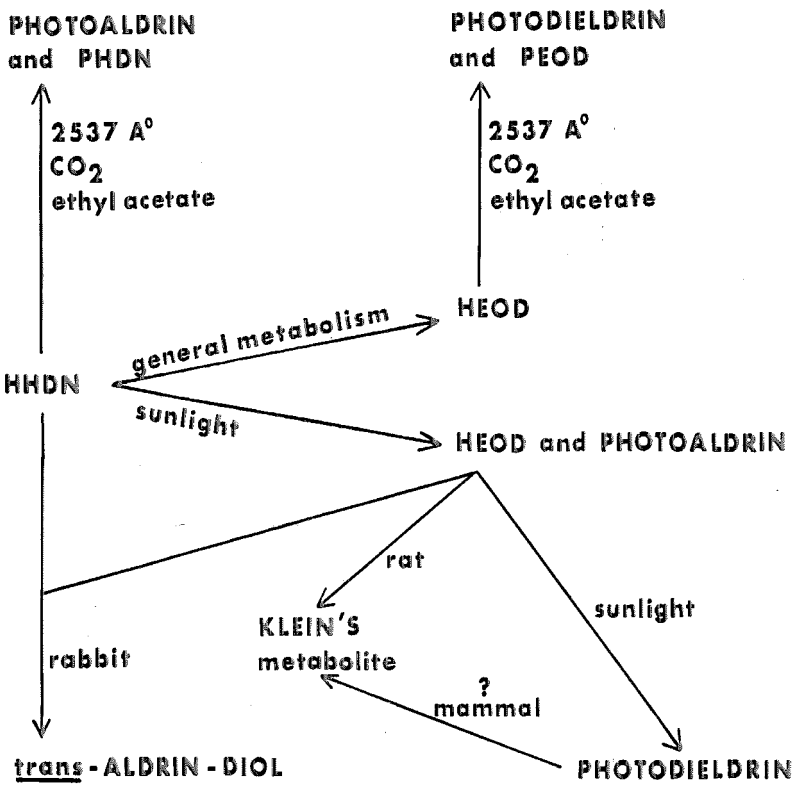

FIG. 1.—The reactions of aldrin and dieldrin.

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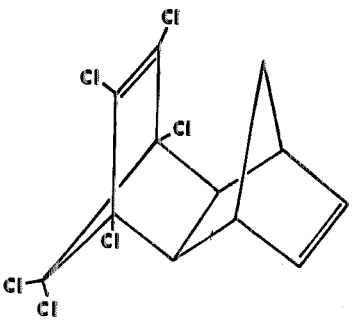
[2] Roman numerals refer to accompanying structural formulae, P. 156.

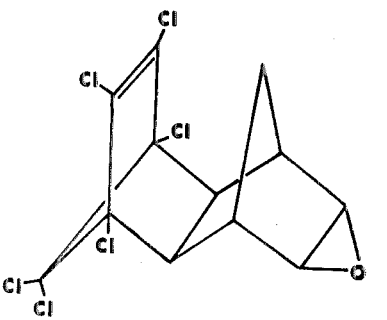
(Damico, Chen, Costello, and Haeni, 1968); and (3) the photoisomerization of aldrin and dieldrin to photoaldrin (1,1,2,3,3a,7a-hexachloro-2,3,3a,3b,4,6a,7,7a-octahydro-2,4,7-metheno-1*H*-cyclopenta(*a*)pentalene) and photodieldrin (1,1,2,3,3a,7a-hexachloro-5,6-epoxydecahydro-2,4,7-metheno-1*H*-cyclopenta(*a*)pentalene) under field and laboratory conditions (Parsons and Moore, 1966; Robinson, Richardson, Bush and Elgar, 1966; Rosen, Sutherland and Lipton, 1966; Rosen and Sutherland, 1967).

Our laboratory has been particularly interested in the photoisomerizations of aldrin and dieldrin to photoaldrin (III) and photodieldrin (IV), processes which occur in sunlight or ultraviolet light (2537°, high energy, short wavelength). These photo reactions may be accomplished in solution or by exposure of the solid insecticide. In solution, the monodechlorinated derivatives (PHDN and PEOD) are also formed, although a recent modification of this reaction results in formation of only the photoisomers (Rosen and Carey, 1968).

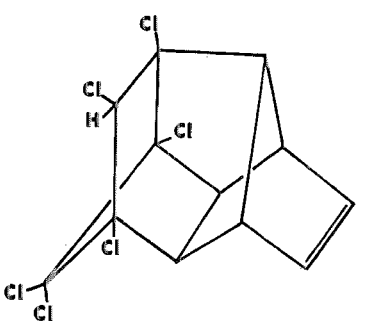
Since photoisomerization of aldrin and



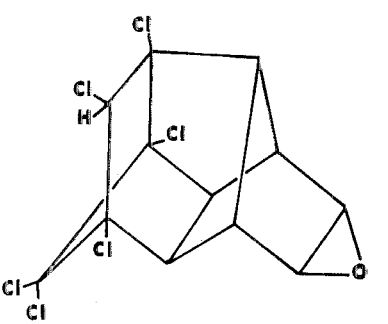
I



II



III



IV

dieldrin can occur in the environment, it is important to determine the toxicities of these photoisomers to various organisms. Previous studies (Rosen, Sutherland and Lipton, 1966; Rosen and Sutherland, 1967) have shown that photodieldrin is more toxic to susceptible and dieldrin-resistant house flies, susceptible mosquito larvae, and mice, and that photoaldrin is more toxic to house flies than aldrin. It appears that at least part of the increased toxicity to insect species is due to a more rapid penetration. Preliminary studies have indicated photoaldrin to be so highly toxic to mosquito larvae as to warrant further investigations of the toxicity to various mosquito species for two reasons, (1) the mosquito as an indicator organism might reveal possible hazards of this photoisomer to other aquatic organisms and (2) photoaldrin might have potential as a practical mosquito larvicide.

MATERIALS AND METHODS. The mosquito species used in these studies were as follows. The *Aedes aegypti* (L.) colony and its susceptibility have been described previously (Sutherland, 1964). A two-hour egg hatch was allowed with subsequent rearing at 29° C., and the populations were sampled at specific times for toxicity assays. Two dieldrin-resistant strains of *A. aegypti* (L.), Isla Verde and Penang, with dieldrin LC_{50}'s of at least 4 p.p.m. were reared in a similar manner and tested as late third and early fourth instar larvae. Three strains of *Culex pipiens pipiens* L. were examined including T.D. and Avalon, field collected as DDT-preresistant and after 18 generations of non-selection reverted to normal DDT susceptibility (DDT LC_{50}'s of 0.042 and 0.06 p.p.m. respectively); and T.D.R., subjected to larval DDT selection for 18 generations. This latter strain is heterogenous and currently its DDT LC_{20} extends as a plateau from 0.5–5 p.p.m. All strains of *C. p. pipiens* were reared at room temperature and tested mainly as fourth instar larvae. *Anopheles stephensi* Liston was reared at room temperature and tested as mixed third and fourth instar.

The WHO method for assaying insecticide resistance (Brown, 1958) was used with slight modifications as previously described (Sutherland, 1964). The compounds, 99 plus percent pure, were dissolved in 95 percent ethanol at the desired concentrations. Each concentration was replicated at least twice in each test, and mortality was determined after 24 and 48 hours. Criterion of larval mortality was failure to fully flex head to siphon when stimulated. Data from tests with susceptible *A. aegypti* were subjected to probit analyses; all other data were plotted on log probit paper, and the regression lines were fitted by eye.

RESULTS AND DISCUSSION. The LC_{50}'s and LC_{90}'s of aldrin and photoaldrin for susceptible *A. aegypti* are given in Table 1 and represent the average of assays on 4–7 separate larval populations of this strain. Photoaldrin consistently is more toxic than aldrin to all larval ages. For newly hatched larvae which generally are not highly susceptible to insecticides and for larvae 24 hours of age when insecticide susceptibility increases, the increased toxicity of photoaldrin is only approximately two-fold. Subsequently, in the later instars the photoisomer is 6.5–11 times as toxic as aldrin. The LC_{50}'s for dieldrin and photodieldrin are 0.0058 and 0.0029 p.p.m. respectively (Rosen, Sutherland and Lipton, 1966), and

TABLE 1.—The LC_{50}'s and LC_{90}'s in p.p.m. of aldrin and photoaldrin for *A. aegypti* larvae.

Compound	LC	Larval age, days				
		Newly hatched	1	2	3	4
Aldrin	50	0.00274	0.000602	0.00163	0.00546	0.00312
	90	0.13828	0.00075	0.00270	0.01025	0.00713
Photoaldrin	50	0.00109	0.00027	0.00033	0.00047	0.00048
	90	0.06693	0.00044	0.00075	0.00092	0.00080

therefore photoaldrin is the most toxic of the two photoisomers. It is also more toxic than Abate (LC_{50} 0.001 p.p.m.) and Dursban (LC_{50} 0.00135 p.p.m.).

Of particular interest in these studies was the possibility that photoaldrin might at least partially circumvent the dieldrin resistance mechanism. However, on the basis of limited tests with the dieldrin-resistant Isla Verde and Penang strains as shown in Table 2, the degree of cross resistance is very high. In fact, based on the characteristic rapid toxic effect of photoaldrin on susceptible insects which implies rapid penetration, the equivalent toxicities of aldrin and photoaldrin to the resistant strains may indicate that resistance in the Isla Verde and Penang strain is due in part to decreased penetration. However, the Isla Verde strain has been shown to absorb as much dieldrin as a susceptible strain, or more (Matsamura and Hayashi, 1966; Khan, 1964). In our studies, although cross resistance to photodieldrin is evident, the relative toxicity of photodieldrin:dieldrin to both the Isla Verde strain and the susceptible strain is approximately the same, 2:1. Possibly resistance to photoaldrin is due to metabolism of this compound by a reaction other than epoxidation to photodieldrin.

Photoaldrin is also highly toxic to susceptible *C. p. pipiens* larvae (Table 3), being 4–5 times as toxic as aldrin. The photodieldrin:dieldrin toxicity ratio is slightly less than that observed with *A. aegypti*. In assays with T.D.R., a strain highly resistant to DDT, the LC_{50}'s of photoaldrin, aldrin, photodieldrin and dieldrin were observed to be 0.00047, 0.0024, 0.002 and 0.004 p.p.m. respectively. This strain is slightly less susceptible than the other strains, but photoaldrin remains highly toxic. The LC_{50} of Abate for the susceptible T.D. strain is approximately 0.0006 p.p.m.

In limited assays with *A. stephensi* the LC_{50} of photoaldrin was 0.002 p.p.m., while at 0.005 p.p.m. aldrin was non-toxic and photodieldrin caused approximately 20 percent mortality.

On the basis of these tests with three species of mosquito, photoaldrin appears to be highly toxic as a larvicide. Currently, nothing is known of its toxicity to other organisms. Preliminary studies on the toxicity of photodieldrin to other animals (Brown, Robinson and Richardson, 1968) indicate that this compound in comparison to dieldrin is more toxic to rats, mice, guinea pigs and pigeons, equally toxic to dogs, and less toxic to domestic fowl and harlequin fish. Experiments of J. Robin-

TABLE 2.—Percent mortality of larvae of 2 strains of dieldrin-resistant *A. aegypti* at 2 and 4 p.p.m. insecticide.

	Time, hr.			
	24		48	
Compound	2 p.p.m.	4 p.p.m.	2 p.p.m.	4 p.p.m.
Dieldrin	22	36(58.7)	48	54(92)
Photodieldrin	..	80(94.3)	..	84(100)
Aldrin	..	42(43)	..	62(54)
Photoaldrin	26	54(41)	42	70(76)

Strains: Isla Verde, (Penang).
Each figure represents the average of 2 replicates.

TABLE 3.—The LC_{50}'s and LC_{90}'s in p.p.m. of aldrin, photoaldrin, dieldrin and photodieldrin for susceptible strains of *C. p. pipiens* larvae.

	Strain		
	T.D.		Avalon
Compound	LC_{50}	LC_{90}	LC_{50}
Aldrin	.001	.0026	.00125
Photoaldrin	.00022	.00056	.00025
Dieldrin	.0015	.0028	.....
Photodieldrin	.00105	.0020	.....

son in 1968 have suggested that photodieldrin is metabolized to Klein's metabolite in some mammals. If photoaldrin also possesses less toxicity for fish, photoaldrin may prove to be highly efficient as a practical mosquito larvicide. In addition, knowledge of the metabolism of this compound may further elucidate the mechanism responsible for dieldrin resistance.

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References Cited

BANN, J. M., DECINCO, T. J., EARLE, N. W., and SUN, Y. P. 1956. The fate of aldrin and dieldrin in the animal body. J. Agr. Food Chem. 4:937–942.

BROWN, A. W. A. 1958. The World Health Organization test kit for detection of resistance in mosquito larvae. Mosq. News 18:128–131.

BROWN, V. K. H., ROBINSON, J., and RICHARDSON, A. 1968. Preliminary studies on the acute and subacute toxicities of a photoisomerization product of HEOD. Fd. Cosmet. Toxicol. 5:(in press).

DAMICO, J. N., CHEN, J. T., COSTELLO, C. E., and HAENNI, E. O. 1968. Structure of Klein's metabolites of aldrin and dieldrin. J.O.A.C. 51:48–55.

GANNON, N., and BIGGER, J. H. 1958. The conversion of aldrin and heptachlor to their epoxides in soil. J. Econ. Entomol. 51:1–2.

KHAN, M. A. Q. 1964. Studies on dieldrin-resistance in *Aedes aegypti* (L.). Ph.D. Thesis. Univ. Western Ontario, Canada.

KORTE, F., and ARENT, H. 1965. Metabolism of insecticides. IX. Isolation and identification of dieldrin metabolites from urine of rabbits after oral administration of dieldrin-^{14}C. Life Sciences 4:2017–2026.

———, LUDWIG, G., and VOGEL, J. 1962. Umwanlung von Aldrin-(^{14}C) und Dieldrin-(^{14}C) durch Mikroorganismen, Leberhomogenate und Moskito-Larven. Liebigs Ann. Chem. 656: 135–140.

LICHTENSTEIN, E. P., and SCHULZ, K. R. 1960. Translocation of some chlorinated hydrocarbon insecticides into the aerial parts of pea plants. J. Agr. Food Chem. 8:452–456.

MATSUMURA, F., and HAYASHI, M. 1966. Interaction of dieldrin with the subcellular components of both resistant and susceptible strains of *Aedes aegypti* L. Mosq. News 26:190–194.

PARSONS, A. M., and MOORE, D. J. 1966. Some reactions of dieldrin and the proton magnetic resonance spectra of the products. J. Chem. Soc. (C):2026–2031.

ROBINSON, J., RICHARDSON, A., BUSH, B., and ELGAR, K. E. 1966. A photoisomerization product of dieldrin. Bull. Environ. Contamination Toxicol. 1:127–132.

ROSEN, J. D., and CAREY, W. F. 1968. Preparation of the photoisomers of aldrin and dieldrin. J. Agr. Food Chem. 16:536–537.

———, SUTHERLAND, D. J. 1967. The nature and toxicity of the photoconversion products of aldrin. Bull. Environ. Contamination Toxicol. 2:1–9.

———, ———, and LIPTON, G. R. 1966. The photochemical isomerization of dieldrin and endrin and effects on toxicity. Bull. Environ. Contamination Toxicol. 1:133–140.

SUTHERLAND, D. J. 1964. Toxicity of insecticides to *Aedes aegypti* larvae. N. J. Mosq. Exterm. Assoc. Proc. 51:107–110.