

Properties of Photoisomers of Heptachlor and Isodrin

The photoisomers of heptachlor and isodrin have been prepared and assayed for insect toxicity. Although the photoisomer of heptachlor exhibits greater toxicity to flies and mosquitoes than heptachlor, a relationship similar to that previ-

ously found for other cyclodiene insecticide photoisomers, the photoisomer of isodrin is less toxic than isodrin. Metabolic studies indicate that this discrepancy is at least partly due to rapid metabolism of the isodrin isomer.

Photoconversion of aldrin (I) and dieldrin (II) to their "half-cage" isomers (III and IV, respectively) results in materials more toxic to mosquitoes (Sutherland and Rosen, 1968) and flies (Rosen and Sutherland, 1967). However, isodrin (V) has been reported to be 2.3 times as toxic to flies as its "birdcage" isomer (VI) (Soloway, 1965). To elucidate further the toxicity relationships between chlorinated cyclodiene insecticides and their "cage" isomers, 1,3,4,5,5a,5b-heptachlorooctahydro-1,2,4-metheno-1H-cyclobuta [cd] pentalene (VII), a possible environmental photoproduct of heptachlor (VIII), was synthesized and its toxicity to two insect species investigated.

Compound VI was also synthesized and assayed for insect toxicity to extend the observations of Soloway (1965).

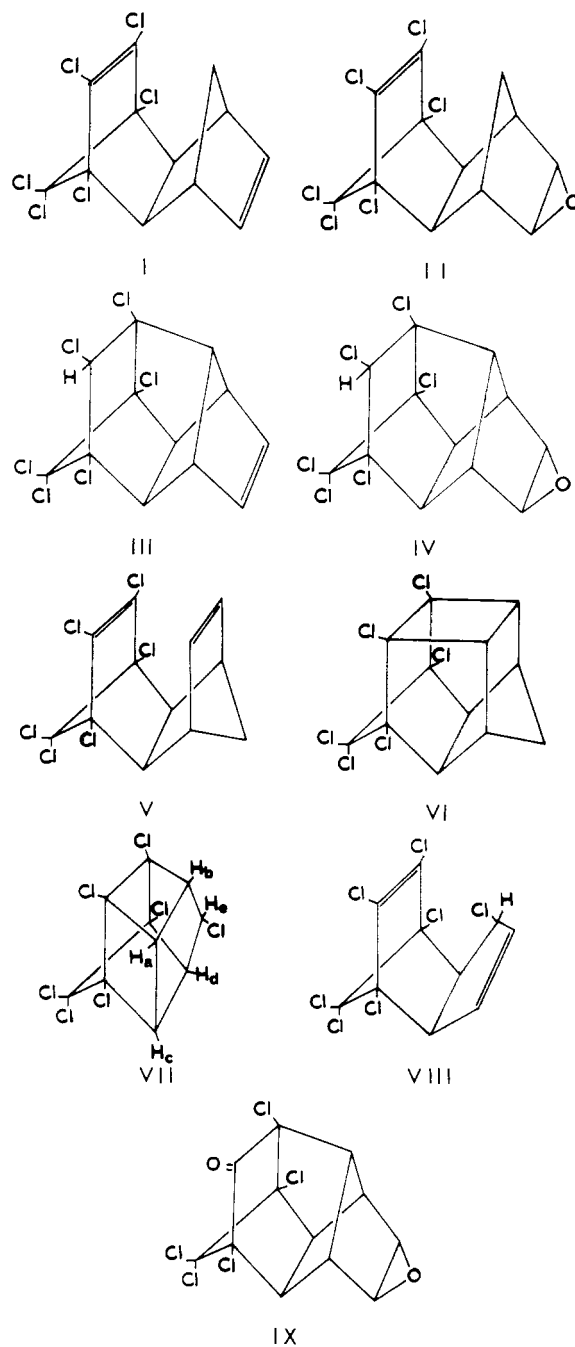
EXPERIMENTAL

Chemicals. Heptachlor, 1,4,5,6,7,8,8-heptachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene, and isodrin, 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4-endo,endo-5,8-dimethanonaphthalene, both 99% pure, were supplied by Velsicol Chemical Corp. and Shell Chemical Co., respectively. Sesamex, 2-(3,4-methylenedioxyphenoxy)-3,6,9-trioxaundecane and sodium barbital were obtained from commercial sources.

Preparation of Photoisomers. Photoisomers VI and VII were prepared by the method previously described for III and IV (Rosen and Carey, 1968). Separation of VI from V and benzophenone sensitizer was achieved by taking advantage of the insolubility of VI in petroleum ether (30° to 60° C.). Recrystallization from ethanol resulted in a 58% yield of material whose infrared spectrum was identical with that of authentic VI (Soloway *et al.*, 1960).

The oil obtained by evaporation of the irradiated heptachlor solution was dissolved in hexane, and VII was separated from heptachlor and benzophenone by preparative thin-layer chromatography on Silica gel G (Stahl) plates. With hexane as eluent, the R_f values of heptachlor, VII, and benzophenone were 0.43, 0.30, and 0.04, respectively. Based on GLC quantitation, the yield of photoheptachlor was 25%. After recrystallization from ethanol, its m.p. was 120–1° C.

Toxicology. The toxicity of compounds to 4-day-old adult flies, *Musca domestica* L., and 3-day-old mos-



quito larvae. *Aedes aegypti* (L.), was determined as previously described (Rosen and Sutherland, 1967). When employed, sesamex (2.5 μ g. per fly) was applied 2.5 hours prior to insecticide treatment, and sodium barbital (0.8% in milk) was fed 24 hours before treatment.

RESULTS AND DISCUSSION

The melting point and TLC R_f value of VII are given in the Experimental section. The GLC retention time at 155° C., other conditions being as previously described (Rosen and Carey, 1968), was 5.8 minutes, as compared with 4 minutes for heptachlor.

The structure of VII has been assigned on the basis of spectroscopic data as well as several reports of analogous photoconversions of *endo*-dicyclopentadiene derivatives to pentacyclo [5.3.0.0^{2,6}.0^{3,9}.0^{5,8}] decanes (Dilling, 1966).

The mass spectrum of VII exhibited a parent ion at m/e 370 and peaks at m/e 270 ($C_5Cl_6^+$) and 100 ($C_5H_5Cl^+$). The intensities of the latter two peaks relative to the rest of the spectrum were less than their relative intensities in the mass spectrum of heptachlor. This can be explained by the argument that these peaks arise by the breaking of four bonds in VII, but only two in heptachlor.

The nuclear magnetic resonance spectrum (in carbon tetrachloride) of VII exhibited ill-defined multiplets centered at 3.45 (Ha-Hd) and 4.78 (He) in the integrated ratio of 4 to 1. Olefin proton absorption of heptachlor at 5.958 was absent in the photoisomer. The infrared spectrum of the photoisomer indicated the absence of chlorinated olefin absorption at 1618 cm^{-1} and thereby further supported the postulated structure.

In toxicity assays (Table I), VII was approximately 2 to 3 times as toxic to flies and mosquitoes as heptachlor, a toxicity-isomerization relationship similar to those of aldrin and dieldrin and their respective photoisomers. However, VI was one-half as toxic as isodrin to flies and one-third as toxic to mosquitoes, thereby confirming the previous results of Soloway (1965).

Pretreatment of flies with sesamex decreased the LD_{50} of VI to 0.032 μ g. per fly. Since sesamex is known to inhibit oxidative functions of microsomes (Brooks and Harrison, 1964), its strong synergistic

effect towards VI suggested that the relatively low toxicity of VI is due in part to its metabolism to less toxic materials. GLC analyses of external washings and homogenates of flies 2.5 hours after insecticide treatment indicated that, while sesamex did not increase initial penetration of VI, the amount of recoverable VI in homogenates of flies pretreated with sesamex was approximately 40% greater than in those not pretreated. Sodium barbital, a stimulator of mammalian microsomal oxidations, caused an approximate 50% decrease in the amount of VI in fly homogenates.

No peak other than that owing to VI was observed by GLC, suggesting metabolism to water-soluble material(s). In contrast to VI, recent experiments (Khan *et al.*, 1968) have indicated that III and IV are metabolized to 1,1,2,3a,7a-pentachloro-5,6-epoxydecahydro-2,4,7-metheno-3H-cyclopenta [a] pentalene-3-one (IX), a material more toxic than dieldrin (Klein *et al.*, 1968). It is impossible for VI to undergo a similar conversion, as it has no secondary chloride group. Such a group is present in VII, and the possible metabolism of VII to a ketone is currently under investigation.

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Table I. Toxicity of Compounds to Insects

Compound	Housefly LD_{50} , μ g./Fly	Mosquito Larvae LC_{50} , P.P.M.
VII	0.0056	0.0015
VIII	0.011	0.0052
VI	0.113	0.058
V	0.054	0.019