Novel Photoproducts of Heptachlor Epoxide, *Trans*-Chlordane, and *Trans*-Nonachlor

by GLEN W. IVIE[1], JOHN R. KNOX, SAFY KHALIFA, IZURU YAMAMOTO[2], and JOHN E. CASIDA

Division of Entomology
University of California
Berkeley, Calif. 94720

The single major photoproduct which has been obtained on exposure of heptachlor epoxide [I, Fig. 1] in acetone solution to ultraviolet light or as thin films to sunlight or a germicidal lamp (1,2) is reported to be the half-cage isomer [IIIA](2), although the isomeric structure [IIIB] also merits consideration (1). Under the same conditions, cis-chlordane [IV] yields a photoproduct which is considered to be the half-cage isomer [VA](2) or one of the two isomeric structures [VA or VB](1). In contrast, no half-cage photoisomers have been isolated following exposure of trans-chlordane [VI] or trans-nonachlor [VIII] to photolytic conditions (1,2,3,4). With these trans compounds, the orientation of the chlorine atom on the center carbon of the cyclopentane ring towards the double bond apparently precludes bridging at this position (1).

This paper describes the nature and toxicity of three novel photoisomers obtained when heptachlor epoxide, trans-chlordane, and trans-nonachlor are exposed to sunlight as deposits on bean foliage, in the presence of rotenone (5), and to ultraviolet light as solutions in acetone. The conversion of heptachlor epoxide to the half-cage isomer [IIIA or IIIB] involves an intermediate [II] which has been isolated and characterized. A new photoisomer of a novel type has also been obtained from each of trans-chlordane and trans-nonachlor.

Materials and Methods

Reference chemicals, analytical procedures, and toxicity tests. Reference samples of compounds I, III, IV, V, VI, and VIII were provided by P. B. Polen (Velsicol Chemical Corp., Chicago, Ill.). The formation of photoproducts was monitored by thin-layer chromatography (TLC) on silica gel F_{254} chromatoplates, using petroleum ether-chloroform mixture (8:1) for heptachlor epoxide and its photoproducts, petroleum ether for cis-chlordane and photo-cis-chlordane, hexane-ether mixture (4:1) for trans-

[1] Present address: Department of Entomology, University of Kentucky, Lexington, Kentucky.

[2] Present address: Department of Agricultural Chemistry, The Tokyo University of Agriculture, Setagaya-ku, Tokyo, Japan.

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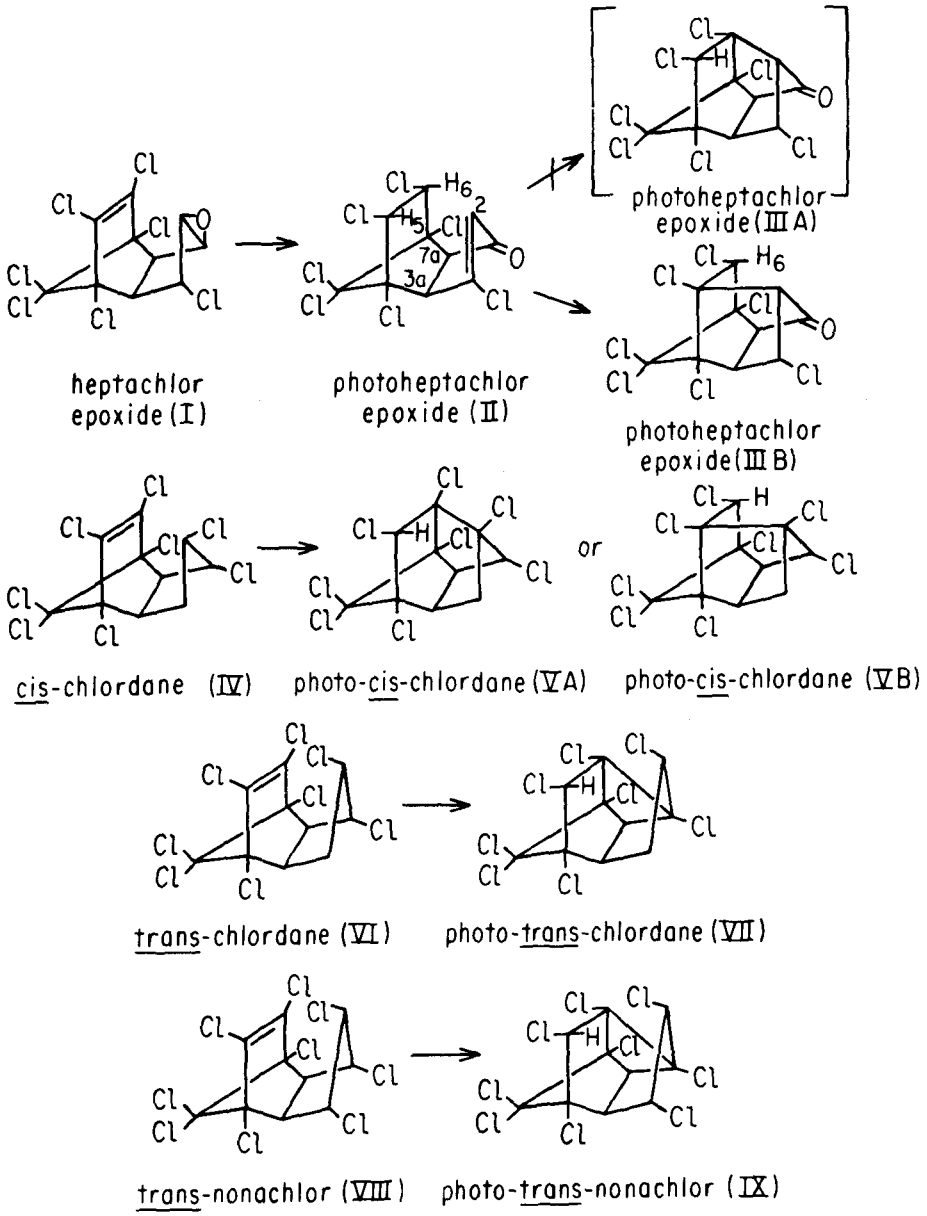
Fig. 1. Structures of heptachlor epoxide [I], cis-chlordane [IV], trans-chlordane [VI], trans-nonachlor [VIII] and some of their possible photoproducts



chlordane and its photoproduct, and hexane-ethyl acetate mixture (20:1) for trans-nonachlor and its photoproduct. Gas-liquid chromatography (GLC) studies were made using a 6-ft x 1/8-in ID glass column packed with 10% DC-200 (viscosity grade 12,500) on 80/100-mesh Gas-Chrom Q with an injection temperature of 225°C and a column and detector temperature of 200°C. Retention times, in minutes, with a nitrogen flow rate of 60 ml/min for the designated compounds were: I - 9.1; II - >120; III - 12.3; IV - 12.0; V - 19.4; VI - 10.7; VII - 24.2; VIII - 12.7; IX - 20.8. Hexadeuterodimethylsulfoxide was the primary solvent used for the proton magnetic resonance (PMR) and ^{13}carbon nuclear magnetic resonance (NMR) studies; however, pentadeuteropyridine and deuterochloroform were also used. The toxicity of the compounds was determined on adult female houseflies of the SCR insecticide-susceptible strain and on male white mice of the Swiss-Webster strain. The flies were used 2-5 days after emergence and they were treated topically, on the thorax, with 1.0 µl of an acetone solution of the test compound; mortality determinations were made 48-hours after treatment. Also, toxicity assays were made with flies pretreated with 5 µg of sesamex synergist dissolved in 1 µl of acetone and applied to the thorax 1 hour before application of the test compound. The mice, weighing approximately 20 g, were treated intraperitoneally with 50 µl of dimethylsulfoxide solution of the test compound; mortality determinations were made 48-hours later.

Preparation and isolation of photoproducts. The photochemical apparatus consisted of a 450-watt, high-pressure, mercury-vapor lamp placed in a water-cooled, double-walled, clear, fused-quartz immersion well. The radiant energy reaching the sample was restricted by a pyrex absorption sleeve which blocked radiation below 280 nm. The cyclodienes (about 4 g in 165 ml of acetone) were irradiated for the respective times necessary to achieve reasonable yields of the photoproducts, which were isolated by chromatography on Florisil columns. With heptachlor epoxide, the irradiation was for 2 hours, followed by chromatographic removal of photoproduct II [eluted with chloroform-hexane mixture (2:1)] and recovery of a mixture of unreacted material and photoproduct III [eluted first with hexane-chloroform mixture (4:1)]. The mixture of heptachlor epoxide and photoproduct III was irradiated again for 2 hours, followed by removal of photoproduct II; this overall procedure was repeated two more times in order to accumulate photoproduct II (an intermediate in formation of photoproduct III). Finally, heptachlor epoxide [I] was separated from photoproduct III by taking advantage of the low solubility of photoproduct III in cold ether. [The final yields were: 13% unreacted heptachlor epoxide; 49% photoproduct II (m.p. 178.5 - 181.5°C, from chloroform-hexane); 26% photoproduct III (m.p. 208 - 209°C, from chloroform-hexane).] cis-Chlordane solutions were irradiated for 48 hours and the photoproduct was separated on Florisil, using petroleum ether for elution and repeating the column purification to obtain pure material (76%, m.p. 148.5 - 151°C, from hexane) and unreacted cis-chlordane (18%). trans-Chlordane was converted to its photoderivative by the same

general procedure and the pure product was obtained after one passage through Florisil with petroleum ether (12%, m.p. 168.5 - 170°C, from hexane). (Recovery of unreacted trans-chlordane was 74%.) trans-Nonachlor was photodecomposed by the same general procedure but three passages through the Florisil column were required to separate unreacted trans-nonachlor (70%) from photoproduct IX (6%, m.p. 154 - 155.5°C, from hexane).

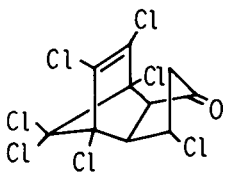
Groups of young bean plants were sprayed to run off with a methanolic solution of the cyclodiene (1% w/v) with or without added rotenone (1% w/v), a potential photosensitizer (5,6). After exposure to sunlight for 4 hours, the plants were rinsed with ether and the rinses were subjected to TLC and GLC analyses.

Results

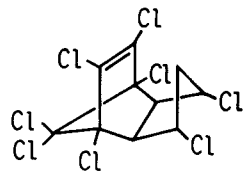
Photoalteration on plant surfaces. The conversion efficiencies of the designated cyclodienes, exposed on rotenone-treated bean leaves to sunlight for 4 hours, were estimated from GLC and TLC analyses to be as follows: 50 - 60% II and 1% III from I; 70 - 80% V from IV; 15 - 20% VII from VI; 15 - 20% IX from VIII. The photoproducts from the plant surfaces are identical (TLC, GLC, IR, and MS) with those formed in acetone solutions exposed to ultraviolet light. No detectable photoproducts were formed in the absence of rotenone as a photosensitizer; so, the reactions on plant foliage are dependent on the presence of the photosensitizer.

Nature of two photoproducts derived from heptachlor epoxide. One of the heptachlor epoxide photoproducts [II] is a precursor for the other one [III] because photoproduct II converts to photoproduct III (identified by TLC, GLC, IR, and MS) in 70% yield when it is exposed in acetone solution to ultraviolet light for 2 hours. On bean leaves exposed to sunlight, rotenone sensitizes the conversion of heptachlor epoxide to photoproduct II but not the conversion of II to photoproduct III; thus, there is a rapid build-up of photoproduct II from heptachlor epoxide in the presence of rotenone, whereas photoproduct III is formed in significant amounts only after prolonged exposure. Direct exposure of photoproduct II to sunlight on plant foliage results in its slow conversion to photoproduct III, but a small amount of photoproduct II remains, even after 7 days.

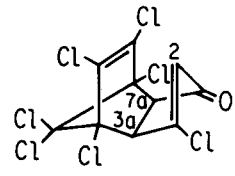
Photoproduct II contains a ketone group (IR) and it is isomeric with heptachlor epoxide and photoproduct III (elemental analysis, MS). One possible isomeric structure [X] is not appropriate because neither of two epimeric chloro compounds formed on reduction of photoproduct II to an alcohol, followed by chlorination, is the same as δ-chlordane [XI]. However, the spectral properties (IR, PMR, ^{13}carbon-NMR, MS), of each of these derivatives and of the photoproduct itself, are consistent with the designated structure for photoproduct II. In particular, three protons (H_2, H_{3a}, and H_{7a}) of photoproduct II have similar chemical shifts and splittings in the PMR spectrum to those of



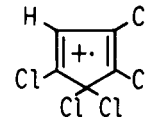
X



δ-chlordane (XI)



XII



XIII

the corresponding protons of the related ketone [XII] of known structure (7); also, the IR and UV spectral absorptions due to the α,β-unsaturated ketone grouping are similar for the two compounds. The hexachlorocyclopentane moiety in photoproduct II is clearly indicated by an AB pattern in the PMR spectrum due to two protons (H_5 and H_6) and by a prominent pentachloro-ion [XIII](m/e 236) in the MS of the alcohol and two chloro derivatives. The ^{13}carbon NMR spectrum of photoproduct II is also consistent with the structural assignment; it shows resonances at the following δ values downfield from tetramethylsilane: 57.7 and 62.3 ppm, each resulting from two ^{13}carbon nuclei; 75.7, 76.2, 99.9, 138.2, 165.3, and 198.6 ppm, each due to single ^{13}carbon nuclei.

Photoproduct III is identical to the compound previously described (1,2), for which structure IIIA (1,2) or structure IIIB (1) has been proposed. Structure IIIB is preferred for photoproduct III because proton H_6 resonates at relatively higher field in the PMR spectrum of the photoproduct than in spectra of related half-cage structures whereas the corresponding signal for the alcohol derived by $NaBH_4$ reduction is at lower field. This is in accord with the anisotropies of the carbonyl and hydroxyl groups. The structure designated [IIIB] for the photoproduct is also preferred to the alternative structure [IIIA] on the basis of a possible intramolecular hydrogen transfer mechanism in the conversion of photoproduct II to photoproduct III.

Nature of photo-trans-chlordane [VII] and photo-trans-nonachlor [IX]. Photo-trans-chlordane is an isomer of trans-chlordane and photo-trans-nonachlor is an isomer of trans-nonachlor (elemental analysis, MS). In each case, a typically low field singlet in the PMR spectrum and the lack of IR absorption due to a disubstituted dichloroethylene grouping indicate that the photoisomers have half-cage structures. Formation of these two photoisomers proceeds slowly relative to the rate of photobridging encountered with cis-chlordane, possibly because a less-accessible hydrogen needs to be abstracted for bridging with the trans compounds; bridging to the central carbon of the cyclopentane ring is precluded by the endo-configuration of the chlorine substituent (1). The PMR spectrum of photo-trans-nonachlor shows it to have structure [IX]. Photo-trans-chlordane gives a closely related PMR spectrum which establishes the similarity of these two photoproducts and, in addition, shows the presence of a methylene group; so, in photo-trans-chlordane, the bridging occurs as shown

in structure [VII].

Toxicity of the photoisomers. The two photoisomers [II and IIIB] of heptachlor epoxide differ markedly in their toxicity to houseflies and, to a lesser extent, mice (Table 1). It is

TABLE 1

Toxicity of Cyclodienes and Photoisomers

Compound (See Fig. 1)	LD_{50}, Mg/Kg		
	Housefly		
	Without Synergist	With Sesamex Pretreatment	Mouse
Heptachlor epoxide [I]	7	7	18
Photo-heptachlor epoxide [II]	>2500	>2500	36
Photo-heptachlor epoxide [IIIB]	2	1	6
cis-Chlordane [IV]	15	15	30
Photo-cis-chlordane [V]	32	28	20
trans-Chlordane [VI]	225	250	130
Photo-trans-chlordane [VII]	>2500	>2500	>1000
trans-Nonachlor [VIII]	75	90	>500
Photo-trans-nonachlor [IX]	550	425	-

interesting that the two-step pathway for heptachlor epoxide photoisomerization shown in Fig. 1 initially involves conversion of the toxicant to an intermediate [II], which has a reduced toxicity to mice and which is completely nontoxic to houseflies, and then to the end product [IIIB], which is more toxic to flies and mice than the parent heptachlor epoxide [I]. Photo-cis-chlordane [V] is approximately half as toxic to flies as the parent cyclodiene but it is slightly more toxic than cis-chlordane to mice. Photo-trans-chlordane [VII] and photo-trans-nonachlor [IX] are essentially nontoxic. Pretreatment with sesamex has little or no effect on the toxicity of these compounds to houseflies (Table 1).

Discussion

The results reported here establish several novel types of

phototransformations for methano-bridged cyclodiene insecticide chemicals. Heptachlor epoxide converts to a compound with an α,β-unsaturated ketone grouping and a dichloroethane moiety, possibly by intramolecular transfer of two hydrogen atoms. The two new functional groups generated allow bridge formation through transfer of one hydrogen atom to yield the half-cage structure. To the best of our knowledge, comparable photochemical reactions have not been reported previously for related compounds. A portion of the final photoisomer yield may arise from photoreaction(s) of heptachlor epoxide not involving the identified intermediate, but the studies were not designed to test this possibility. The transformations occuring with trans-chlordane and trans-nonachlor appear to be novel, also, because the half-cage products contain a four-membered ring system rather than the five-membered ring system present in the half-cage products derived from related compounds.

The photoisomers of heptachlor epoxide, cis-chlordane, trans-chlordane, and trans-nonachlor are probably of little importance in evaluating the significance of environmental residues associated with the use of heptachlor and chlordane as insecticide chemicals. The photoisomers are not expected to form in appreciable amounts in the environment unless a potent photosensitizer is present. Further, these studies suggest that the small quantities of photoisomer residues that might occur do not pose a hazard, from a toxicological standpoint.

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