

Table III. NMR Parameters

Compd no.	Solvent	$\Delta\nu$, Hz	T_c , °C	ΔG^\ddagger , kcal/mol ^b
5	ODCB ^a	14.0	52	16.8
6	ODCB	13.7	61	17.3
7	ODCB	32.1	93	18.4
8	ODCB	30.7	102	18.9

^a *o*-Dichlorobenzene. ^b ΔG^\ddagger was calculated according to the following equation (Rauk et al., 1970):
 $k_c = (\pi/\sqrt{2})\Delta\nu = (kT_c/h)e^{-\Delta G^\ddagger/RT_c}$.

alent. The coalescence temperature (T_c), the chemical shift separation ($\Delta\nu$), and the free energy of activation (ΔG^\ddagger) of carbamoyl sulfoxides and sulfones are listed in Table III. The coalescence temperatures for carbamoyl sulfoxides are in the range of 52–61 °C and those of carbamoyl sulfones, 93–102 °C. The coalescence temperatures of thiocarbamates are generally in the range of –1 to 7 °C, except for *S*-ethyl hexahydro-1*H*-azepine-1-carbothioate (Ordram), which is 35 °C (Rummens and Louman, 1970). The increase in the barrier of rotation about the amide C–N bond on oxidation of the thiocarbamate to its corresponding sulfoxide and sulfone is believed to be due to the increase in the contribution of the zwitterion structure VI.

Most of the carbamoyl sulfoxides do not give measurable molecular ions in their mass spectra. In each structure studied in the molecular ion, if observed at all, was much less than 0.1% of the base peak. In each case $P^+ \cdot -O$ was observed at abundances of about 0.1 to 0.6%. The

fragmentation patterns are quite similar to those of the precursor thiocarbamates, i.e., the base peak is R'_2NCO^+ (or occasionally R^+), with major peaks at $R'NHCO^+$, R^+ , R^+ , and, at lower abundance, RS^+ and RS^+H .

One feature, unique to the sulfoxides, is the existence of peaks with masses corresponding to RSO^+ or $RSOH^+$ in fair abundance (ca. 1 to 8%). Compound 2 is an exception to these rules; most of the fragments above the 1% level arise from the precursor ion, VII, presumably because of the additional stabilization arising from the ring system.

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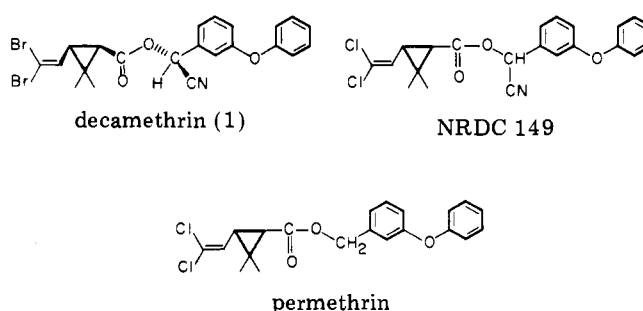
Pyrethroid Photochemistry: Decamethrin

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Photolysis of (*S*)- α -cyano-3-phenoxybenzyl *cis*-(1*R*,3*R*)-2,2-dimethyl-3-(2,2-dibromovinyl)cyclopropanecarboxylate (decamethrin) in various solvents using ultraviolet radiation ($\lambda > 290$ nm) results initially in *cis*-*trans* isomerization, ester cleavage reactions, and loss of bromine. *Cis*-*trans* isomerization is the major reaction of sunlight irradiation in the solid phase on glass or silica gel. An additional process for dilute solutions in methanol exposed to sunlight involves racemization at the α position in the alcohol moiety by both photochemical and ground-state reactions. Twenty-five photoproducts are identified from irradiation of decamethrin or its initial photolytic derivatives. The effects of quenchers, sensitizers, and solvent viscosity on the reaction rate and product distribution implicate processes in decamethrin photodecomposition that include both singlet and triplet excited states and sometimes "cage" type intermediates. Decamethrin undergoes photolysis more readily than two related pyrethroids, NRDC 149 and permethrin. The mixtures of decamethrin photoproducts from solution and solid-phase reactions are less toxic than decamethrin to mice treated intraperitoneally.

Decamethrin (1) (also known as Decis and NRDC 161) is the most potent insecticide currently known (Elliott et al., 1974a,b, 1975). The *cis*-1*R*,3*R* configuration about the cyclopropane ring and the *S* configuration for the cyano group at the benzylic carbon are essential features for this remarkable insecticidal activity (Elliott et al., 1974a,b, 1975; Owen, 1975). Related but less insecticidal compounds of interest are NRDC 149 (Elliott et al., 1975) and permethrin (Elliott et al., 1973).

The available knowledge on pyrethroid photochemistry (Elliott and Janes, 1973; Holmstead et al., 1977) and



toxicology is not sufficient to predict the photolytic fate of decamethrin and the persistence and biological activity of its photoproducts. The variety of functional groups in 1 poses challenging aspects in its photochemistry as re-

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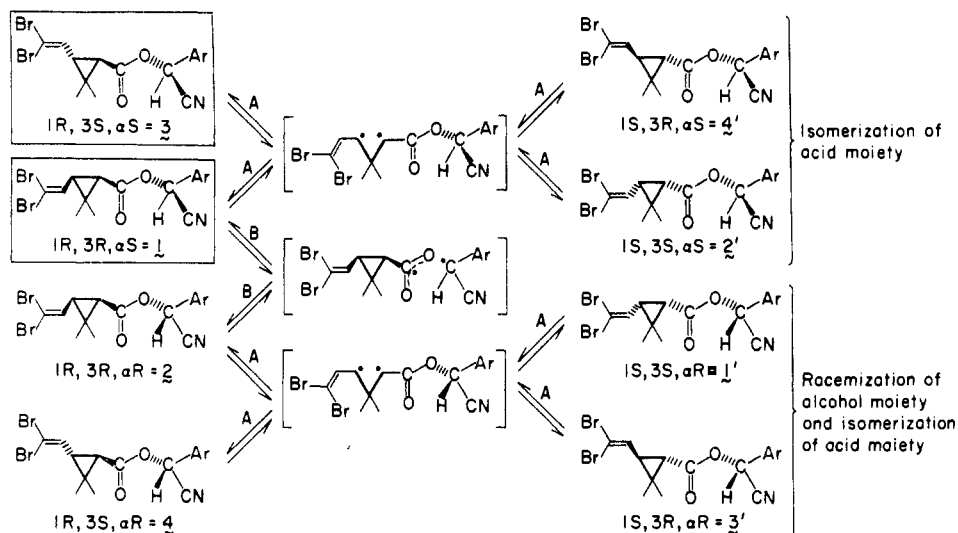


Figure 1. Photochemical pathways and processes (A, B) for interconversion of the eight decamethrin isomers. Structures for the most biologically active isomers are shown in rectangles. Each pair of optical antipodes (i.e., 1 and 1', 2 and 2', etc.) is not separated by the GLC and TLC conditions used. Possible radical intermediates are shown in brackets.

ported in our preliminary communication (RuZO et al., 1976) and detailed here.

MATERIALS AND METHODS

Spectroscopy. Ultraviolet (UV) spectra were determined using the Bausch and Lomb Spectronic 505 double-beam UV spectrophotometer. Infrared (IR) spectra were recorded as KBr pellets unless otherwise specified with the Perkin-Elmer Model 457 grating IR spectrophotometer. Nuclear magnetic resonance (NMR) spectra were obtained with the Perkin-Elmer R32B 90 MHz spectrometer using samples dissolved in deuteriochloroform containing 1% tetramethylsilane (Me_4Si) as internal standard. Chemical shifts (δ) are reported in parts per million (ppm) downfield from Me_4Si and coupling constants (J) are given in hertz (Hz).

Mass spectra (MS) were recorded on a Finnigan Model 1015D mass spectrometer in combination with a System Industries Model 150 control system. The spectrometer was coupled to a Finnigan Model 9500 gas chromatograph operated with temperature programming (120–300 °C, 10 °C/min) using He as carrier gas (20–25 mL/min). Methane was the reagent gas with a chemical ionization (CI) source pressure of 0.5–1.0 Torr.

Chromatography and Analyses. Gas chromatography (GC) for photoproduct quantitation utilized a Varian Aerograph Series 1400 instrument equipped with a flame ionization detector and a glass column (2 m \times 3 mm i.d.) of 3% Dexil on Varaport 30 (80–100 mesh). The column temperature was programmed (120–300 °C, 10 °C/min) with He as carrier gas (20–25 mL/min). Detector and injection port temperatures were 310 °C. Individual peak areas on GC of photolysis mixtures were compared with those for known amounts of authentic standards or, when standards were not available, the quantitation was based on peak area comparisons with known amounts of standards with similar retention times (t_R).

Thin-layer chromatography (TLC) was carried out with precoated 20 \times 20 cm chromatoplates as follows: silica gel 60 F-254 (fluorescent indicator) with 0.25 mm gel thickness (EM Laboratories, Inc., Elmsford, N.Y.) for analytical studies; silica gel GF with 1 mm gel thickness (Analtech, Inc., Newark, Del.) for preparative isolations. Four TLC solvent systems were employed: (A) *n*-hexane-ether (4:1); (B) benzene-carbon tetrachloride (1:1); (C) benzene-chloroform (1:1); (D) benzene (saturated with formic

acid)-ether (10:3). Two-dimensional TLC involved three developments in the first direction with solvent system A followed by two developments in the second direction with B (i.e., A \times 3, B \times 2). The resolved products were detected by their quenching of gel fluorescence under short wavelength UV light or by the blue or red color obtained on spraying with 20% (w/v) phosphomolybdic acid in ethanol, followed by heating at 110 °C for 10 min. Radioactive gel regions detected by radioautography were scraped free from the glass support for liquid scintillation counting (LSC) or for product recovery by extraction of the gel with chloroform, methanol, or other solvents as specified, followed by cochromatography with unlabeled standards.

Column chromatography utilized a column (32 cm \times 4 cm i.d.) containing 150 g of Florisil (60–100 mesh) (Floridin Co., Berkeley Springs, W. Va.) packed in hexane. It was developed with 200 mL each of hexane and various ether in hexane mixtures (i.e., 10, 20, 30%, etc.), followed by ether (500 mL) and methanol (500 mL). Each fraction (20 mL) was inspected by TLC and GC and combined with adjacent fractions of similar composition. Further purification was by preparative TLC.

Synthesis or Sources of Standards. The compounds are designated as shown in Figures 1 and 2. Roussel-Uclaf-Procida (Paris, France) supplied unlabeled 1 and three labeled preparations of this compound (>99% optical and radiochemical purity) with ^{14}C in the cyano (^{14}CN), benzylic ($^{14}\text{C}_\alpha$), and dibromo-substituted ($^{14}\text{C}_\nu$) carbons. They also provided compounds 2, 9 and 18 and various isomer mixtures (1 + 2, 1' + 2', 3 + 4, 3' + 4'). Other standard compounds (5–7, 11, 12, 14, 17, 20–23) were prepared as indicated below. The chromatographic and GC properties of these compounds are given in Tables I and II, the latter of which provides similar data on photoproducts not available as standards from synthesis. The IR and NMR spectral properties are discussed below for critical compounds.

In the decamethrin isomers the IR bands for C=O and CN appear at 1740 and 2220 cm^{-1} while the characteristic NMR signals are given in Table I.

Monobromo esters 5 and 6 were obtained in a 4:1 ratio and in 42% overall yield by treatment of 1 (1.0 g, 2.0 mmol) with triphenyltin hydride (0.7 g, 2.0 mmol) (Kuivila and Menapace, 1963) in benzene (1.0 mL) on irradiation of the mixture with UV light ($\lambda > 290 \text{ nm}$). The products

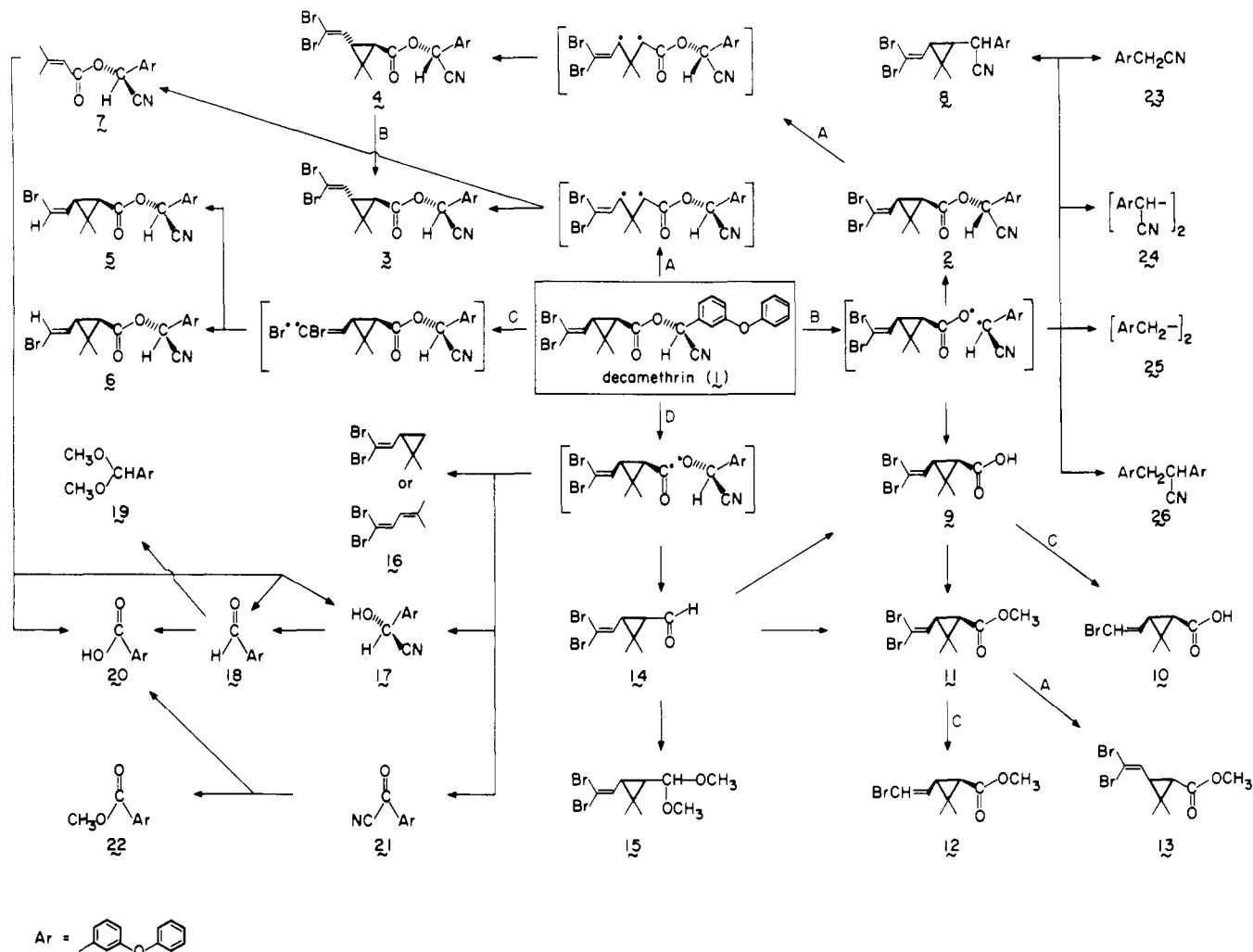


Figure 2. Photochemical pathways and processes (A–D) for decamethrin at 30–50% conversion giving compound designations. Possible radical intermediates are shown in brackets.

were separated by TLC (A × 2). Compound 5: NMR δ 7.0–7.5 (m, 9), 6.46 (dd, 1, $J = 7.2, 2.0$), 6.35 (s, 1), 6.29 (d, 1, $J = 7.2$), 2.31 (t, 1, $J = 8.8$), 1.90 (d, 1, $J = 8.8$), 1.30 (s, 3), and 1.22 ppm (s, 3). Anal. Calcd for $C_{22}H_{20}BrNO_3$: C, 61.99; H, 4.73; Br, 18.75; N, 3.28. Found: C, 61.82; H, 4.70; Br, 19.10; N, 3.10. Compound 6: NMR δ 7.0–7.5 (m, 9), 6.49 (dd, 1, $J = 14.0, 8.7$), 6.39 (s, 1), 6.18 (d, 1, $J = 14.0$), 1.95 (dd, 1, $J = 13.5, 8.7$), 1.82 (d, 1, $J = 8.7$), 1.23 (s, 3), and 1.19 ppm (s, 3). Found: C, 61.86; H, 4.65; Br, 19.30; N, 3.04.

To prepare compound 7, 3,3-dimethylacrylic acid (0.4 g, 4 mmol) was reacted with thionyl chloride (0.5 g, 4 mmol) in benzene (5.0 mL) to give the acid chloride which in turn was coupled with the cyanohydrin (17, see below) (0.8 g, 3.5 mmol) in benzene (5.0 mL) by addition of pyridine (0.5 g). Purification by TLC (C) yielded 7 in 34% yield. NMR δ 7.0–7.5 (m, 9), 6.42 (s, 1), 5.75 (m, 1), 2.21 (s, 3), and 1.93 ppm (s, 3). Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.26; H, 5.58; N, 4.55. Found: C, 74.28; H, 5.59; N, 4.60.

Compound 9 exhibits NMR signals at δ 7.48 (s, 1), 6.75 (d, 1, $J = 7.9$), 2.04 (q, 1, $J = 7.9$), 1.89 (d, 1, $J = 7.9$), 1.30 (s, 3), and 1.22 ppm (s, 3). It gives IR bands at 1690 (C=O) and 3080 cm^{-1} (OH). Its methyl ester (11) (mp 59–61 °C from ethanol), formed quantitatively on reacting 9 with diazomethane in ether, gave NMR signals at δ 6.81 (dd, 1, $J = 7.8, 1.2$), 3.69 (s, 3), 2.04 (q, 1, $J = 7.8$), 1.89 (d, 1, $J = 7.8$), 1.32 (s, 3), and 1.30 ppm (s, 3).

The two monodebromo acids (10) were prepared as their

methyl esters (12) in a 1:1 ratio and in 40% overall yield by treatment of 11 (1.0 g, 3.2 mmol) with triphenyltin hydride (3.5 g, 10 mmol) in benzene (5.0 mL) by irradiation of the mixture with UV light ($\lambda > 290$ nm). The two products were separated from starting ester and from each other by preparative GC (dexil column as for analysis, 150 °C). The NMR spectrum of the *cis*-debrominated ester showed the following NMR signals: δ 6.53 (dd, 1, $J = 7.2, 2.0$), 6.31 (d, 1, $J = 7.2$), 3.80 (s, 3), 2.23 (t, 1, $J = 8.7$), 1.88 (d, 1, $J = 8.7$), and 1.30 ppm (s, 6). Anal. Calcd for $C_9H_{13}BrO_2$: C, 46.38; H, 5.62; Br, 34.28. Found: C, 46.22; H, 5.80; Br, 34.28. The *trans*-debrominated isomer had NMR δ 6.60 (dd, 1, $J = 13.5, 2.0$), 6.18 (d, 1, $J = 13.5$), 3.80 (s, 3), 1.60–2.10 (m, 2), 1.32 (s, 3), and 1.22 ppm (s, 3). Anal. Found: C, 46.10; H, 5.71; Br, 34.46.

Aldehyde 14 was prepared via the corresponding ester and alcohol by reaction of 11 (50 mg, 0.16 mmol) in dry tetrahydrofuran (1 mL) with $LiAlH_4$ (30 mg, 0.8 mmol) at 25 °C on stirring for 4 h. The resulting alcohol, obtained in 88% yield and consisting of approximately equal amounts of *cis* and *trans* material, gave NMR signals at δ 6.08 (d, 1), 3.71 (t, 2), 2.96 (s, 1), 1.4–1.9 (m, 2), and 1.12 ppm (s, 6). The small amount of ester material recovered from several runs consisted of both 11 and its isomer, compound 13. The isomeric alcohols (40 mg, 0.14 mmol) were oxidized with CrO_3 (100 mg, 1.0 mmol) in dichloromethane (1.5 mL) containing pyridine (140 mg) (Ratcliffe and Rodehorst, 1970). The aldehyde 14 was isolated in 74% yield by TLC (A × 2) and characterized

Table I. Analytical Data for Decamethrin Isomers

Compd	TLC R_f values in indicated solvent systems		Nmr chemical shifts, δ ppm, and coupling constants, Hz					
	A \times 3	B \times 2	H_a	H_b	H_c	$H_{d,e}$	H_f	H_g
1	0.74	0.62	6.72 (d, $J = 7.8$)	2.12 (dd, $J = 7.8$)	1.94 (d, $J = 7.8$)	1.22 (s) 1.28 (s)	6.40 (s)	7.0-7.5 (m)
2	0.81	0.63	6.69 (d, $J = 7.8$)	2.07 (dd, $J = 7.8$)	1.90 (d, $J = 7.8$)	1.29 (s) 1.31 (s)	6.36 (s)	7.0-7.5 (m)
3 ^a	0.69	0.50	6.18 (d, $J = 7.8$)	2.26 (dd, $J = 7.8, 5.6$)	1.71 (d, $J = 5.6$)	1.20 (s) 1.26 (s)	6.41 (s)	7.0-7.5 (m)
4 ^a	0.74	0.50	6.16 (d, $J = 7.8$)	2.23 (dd, $J = 7.8, 5.6$)	1.69 (d, $J = 5.6$)	1.23 (s) 1.34 (s)	6.40 (s)	7.0-7.5 (m)

^a The trans-(1R,3S) isomer with higher toxicity to houseflies is assigned the α -(S) configuration (i.e., 3).

from its NMR spectrum: δ 10.25 (s, 1), 6.38 (d, 1, $J = 7.8$), 2.0-2.4 (m, 2), 1.36 (s, 3), and 1.28 ppm (s, 3). Anal. Calcd for $C_8H_{10}Br_2O$: C, 34.08; H, 3.57; Br, 56.68. Found: C, 34.60; H, 3.51; Br, 56.60.

Cyanohydrin 17 was obtained by addition of 18 (3.4 g, 17 mmol) to a suspension of sodium cyanide (23 mmol) in ethanol (20 mL) and acetic acid (2.0 mL) at -10°C . The mixture was stirred for 1 h at -10°C and 2 h at 45°C and then poured into water (150 mL). The cyanohydrin, recovered in 82% yield by extraction into ether, was used without further purification. It is unstable and upon prolonged exposure to air is converted to the aldehyde. The IR spectrum showed 3420 (OH) and 2240 cm^{-1} (CN). Anal. Calcd for $C_{14}H_{11}NO_2$: C, 74.71; H, 4.93; N, 6.22. Found: C, 75.01; H, 4.72; N, 5.87.

Compound 18 gave NMR signals at δ 10.03 (s, 1) and 7.3-7.7 ppm (m, 9) and an IR band at 1706 cm^{-1} (C=O).

3-Phenoxybenzoic acid (20) was obtained almost quantitatively by oxidation of 18 (1.0 g, 5 mmol) in acetone (25 mL) by addition of $KMnO_4$ (1.0 g, 6.3 mmol) in water (5.0 mL). Excess $KMnO_4$ was destroyed by addition of 2-propanol, the reaction mixture was filtered and the filtrate acidified to pH 3 (HCl). The acid (20) recovered by extraction with ether was recrystallized (mp 149°C) from benzene. The methyl ester (22) was prepared in essentially quantitative yield by reaction of 20 with diazomethane in ether. This ester exhibited NMR signals at δ 7.0-7.8 (m, 9) and 3.95 ppm (s, 3) and an IR band at 1720 cm^{-1} (C=O).

To prepare the benzoyl cyanide (21), a solution of 20 (1.0 g, 4.6 mmol) in benzene (5.0 mL) was refluxed with $SOCl_2$ (1.0 g, 8 mmol) for 2.5 h. After solvent evaporation the acid chloride was reacted at $150-230^\circ\text{C}$ with excess CuCN (Oakwood and Weisgerber, 1944) for 4 h. The product was recovered in 39% yield on extraction with hexane and TLC purification ($A \times 2$). The IR spectrum (CCl_4) showed 1790 cm^{-1} (C=O) and 2240 cm^{-1} (CN). Anal. Calcd for $C_{14}H_9NO_2$: C, 75.33; H, 4.06; N, 6.27. Found: C, 75.62; H, 4.00; N, 6.16.

The benzyl cyanide (23) was prepared via 3-phenoxybenzyl chloride obtained according to the general procedure of Zweifel et al. (1970) by reacting 3-phenoxybenzyl alcohol (20 g, 100 mmol) (Aldrich Chemical Co., Milwaukee, Wis.) in ether (50 mL) containing tributylamine (18.9 g, 102 mmol) with $SOCl_2$ (13.3 g, 113 mmol), refluxing for 30 min, followed by removal of the reflux condenser, further addition of $SOCl_2$ (1.6 g, 13.2 mmol), and maintaining the temperature at 80°C for 1 h. Ice was added to the reaction mixture and 3-phenoxybenzyl chloride was recovered in essentially quantitative yield on extraction with ether. This chloride (22.0 g, 100 mmol) in acetonitrile (50 mL) was treated with excess potassium cyanide and refluxed for 6 h. On addition of water and extraction with ether, 23 was recovered in nearly quantitative yield. It gave an IR band at 2225 cm^{-1} (CN).

Irradiation Procedures. Compound 1 in solution or in the solid phase was irradiated with sunlight or with UV light (λ 290-320 nm). The procedures indicated below for 1 are also applicable to some of its initial photoproducts which were individually irradiated under comparable conditions.

Sunlight Irradiation. Following exposure of 1 (3 mg/cm²) on glass or silica gel 60 chromatoplates to bright sunlight for 30 h, the photolyzed material was recovered by washing the glass surface with chloroform (>95% recovery) or by extraction of the gel with ether (~70% recovery). The product mixture was analyzed by GC and fractionated by column chromatography and TLC to

Table II. Characterization and Quantitation of the Decamethrin Photoproducts

Product desig. ^a	Product yield, % ^b			GLC <i>t</i> _R , min	TLC <i>R</i> _f values in indicated solvent systems			CI-MS (methane), [M + 1] ⁺ , <i>m/e</i> (rel intensity) ^c
	Methanol	Hexane	Acetonitrile- water		Solid	A × 2	B	
1								
3 + 4'	~4		11	32	0.66	0.52	0.88	504 (69)
					0.61	0.43	0.82	504 (71)
					0.66			
5	16	12	5					426 (59)
6	~4							426 (61)
7	~4		4	6	0.59	0.56	0.71	309 (89)
8	~4		~4	~4				460 (87)
9	11	20	13	10				297 (87)
10	~4	2	6					219 (90)
11	7							311 (92)
12	~4							233 (76)
13	~4							
14	~4							281 (62)
15	~4							327 (5)
16	~4							253 (96)
17	{ 8	12	29	24				199 (96)
18								245 (2) [213 (68)]
19	2							215 (91)
20	2		22					224 (5) [197 (74)]
21								229 (92)
22	24							210 (59)
23	6	3	6					417 (14)
24	0		{ 0	0				367 (14)
25	0	~18	{ 0	0				392 (14)
26	0		{ 0	0				

^a See Figures 1 and 2 for structures. ^b Yields are percent (molar equivalent basis) of total product formation at 30-50% conversion based on GC analysis using λ 290-320 nm irradiation for solutions and sunlight for solid-phase reactions. The total identified products in methanol, hexane, acetonitrile-water, and the solid phase, respectively, are as follows: products containing the acid moiety, 62, 34, 43, and 52%; products containing the alcohol moiety, 70, 67, 81, and 66%. ^c Assignments given only for the most abundant isotopes in the ion clusters.

obtain the individual pure components for more detailed analysis. Similar conditions were used for exposing [^{14}C]1 on glass ($40\ \mu\text{g}/\text{cm}^2$; 4 or 8 h) and for product recovery and two-dimensional TLC analysis. The resolved ^{14}C products were extracted from the gel with chloroform (>90% recovery) and quantitated by LSC.

Solutions of [^{14}C]1 ($8.0 \times 10^{-4}\ \text{M}$) in methanol, ethanol, or 1-propanol (spectrograde) with or without isobutyrophenone (0.17 M) were exposed to sunlight through quartz for 2 or 8 days. The ^{14}C products were analyzed as above.

Ultraviolet Irradiation. A Rayonet reactor (The Southern N.E. Ultraviolet Co., Middletown, Conn.) was used with RPR 3000 lamps (peak output λ 290–320 nm). Solutions of unlabeled 1 ($8.0 \times 10^{-3}\ \text{M}$ unless indicated otherwise) in methanol, hexane, or acetonitrile–water (3:2) were contained during photolysis in sealed borosilicate glass tubes (UV cutoff $\lambda < 290\ \text{nm}$). The tubes were placed in a “merry-go-round” arrangement within the reactor, thus insuring equal exposure of all samples during the 6–10-h irradiation. In all cases “dark” samples were kept as controls. For analysis, the solvent was evaporated or, in the case of aqueous acetonitrile, diluted with an equal volume of water and extracted first with hexane and then with ether (>90% recovery). The mixtures were analyzed by GC, with product quantitation where feasible, and by GC–MS and TLC before and after methylation (diazomethane). Finally they were fractionated by column chromatography and preparative TLC. The trans isomers of 1 (i.e., 3 and 4') were quantitated directly in the mixture by comparisons of the areas obtained in the NMR spectra for the vinyl proton (Table I).

In separate studies determining the extent of photolysis during 6-h irradiation, 1 ($4.5 \times 10^{-3}\ \text{M}$) was examined in various solvents with or without quenchers and sensitizers ($1.0 \times 10^{-2}\ \text{M}$) and 1, NRDC 149 and permethrin (each at $1.0 \times 10^{-3}\ \text{M}$) were intercompared in methanol solutions.

Characterization of Photoproducts. The identity of individual photoproducts from unlabeled 1 was established by comparison with the standards as follows: cochromatography by GC and TLC and identical NMR and GC–MS, 2, the trans isomers of 1 (i.e., 3 + 4'), 5, 7, 9, 11, 18, 22; cochromatography by TLC and GC and identical MS, 12, 20, 21, 23; cochromatography by GC and identical GC–MS, 6, 14; cochromatography by TLC and identical MS, 17. The other photoproducts (8, 10, 13, 15, 16, 19, 24–26) were tentatively identified by GC–MS (Table II). In addition, the structural assignment for photoproduct 19 was supported by NMR [δ 6.9–7.4 (m, 9), 5.38 (s, 1), and 3.34 ppm (s, 6)]. The ^{14}C photoproducts from sunlight irradiation of [^{14}C]1 were identified by two-dimensional TLC cochromatography with 2, 3, 4, 9, 17, and 18.

Toxicity Assays. The authentic standards or fractions from photodecomposed 1 were administered intraperitoneally (ip) in methoxytriglycol to male albino mice as previously described (Ueda et al., 1974) for 24-h LD₅₀ determinations. Six authentic standards were assayed with normal mice and mice pretreated with piperonyl butoxide (PB, an oxidase inhibitor) (150 mg/kg ip, 1-h pretreatment) or *S,S*-tributyl phosphorotrithioate (DEF, an esterase inhibitor) (50 mg/kg ip, 6-h pretreatment). Two individual photoproducts (9, 20) and fractions from photodecomposed 1 were tested with normal mice only. The photoproduct mixtures were generated by exposing 1 in the solid phase on glass to sunlight for 8 days and in acetonitrile–water (3:2) solution to UV light for 24 h. The solid-phase photoproducts were dissolved in acetonitrile–water (3:2) and extracted first with hexane and then with ether, as for the solution photoproducts. Times were

selected to give 50% of the product mixture as 1 and isomerized derivatives and 50% as polar products.

RESULTS

Photoproducts from Sunlight Irradiation of Solutions or Solid Phases. Unlabeled 1 in thick films on glass yields as major photoproducts the trans isomers (3 + 4') and compounds 9 and 17 plus 18 (Table II). Small amounts of 7 and 8 are detected (Table II) as is also the *trans*-dibromovinyl acid (GC–MS). Photolysis of 1 on silica gel proceeds more slowly but gives the same products. Two other photoproducts show GC–MS quasimolecular ion clusters at m/e 520 and 536 and higher t_R values than starting material; these photoproducts presumably arise by oxidation of 1. Most of the additional photoproducts on glass are polar materials [very low R_f values on TLC (D); elute from the Florisil column with methanol but not with ether]. On methylation (diazomethane) this mixture yields 12 bands of higher R_f on TLC (D). The two major fractions were purified for further analysis. The lower R_f band (0.47) shows NMR signals at δ 7.0–7.5 (m, 9), 6.32 (s, 1), 4.86 (d, 1, $J = 11.0$), 3.81 (s, 3), 1.90 (m, 2), and 1.21 ppm (d, 6), and the higher R_f band (0.52) gives an identical spectrum except for a downfield shift in the signal at δ 6.32 to 6.42 ppm. Their IR spectra closely resemble that of 1 and they give quasimolecular ion clusters at m/e 527 on direct probe MS analysis.

[^{14}C]1 as a thin film on glass yields mainly the trans isomers (3 and 4'), and there are smaller amounts of various cleavage products (9, 17, 18) and polar materials (Table III). The trans isomers (3, 3', 4, 4') and cleavage products are also obtained in methanol; however, the predominant product is 2 (Table III) as confirmed by NMR on the isolated unlabeled product.

The rate of disappearance of [^{14}C]1 and the yield of its epimer 2, the major product, decrease in the solvent order of: methanol = ethanol > 2-propanol (Table IV). Only a portion of the formation of 2 in methanol is attributable to photochemical processes. Isobutyrophenone sensitizes the photoisomerization reaction, i.e., conversion of 1 to its trans isomers (3, 4').

The dimethylacrylate 7 photodecomposes slowly in methanol (~10% overall conversion on 30-h irradiation) and only products arising from the alcohol moiety are detected by GC–MS. Greater than 80% of the total product formation is due to 17, 18, and 22 while small amounts of 19 and 23 are also present. Photolysis of 7 proceeds slowly on glass (5% in 14 days) and the only products detected are 17 and 18. The cyanohydrin (17) on glass photolyzes exclusively to the aldehyde (18).

Photoproducts from Ultraviolet Irradiation of Solutions. General Characteristics. The photodegradation rate of 1 decreases with increased solvent viscosity as evident on comparing hexane and cyclohexane and supported by the findings on polar solvents (i.e., methanol > ethanol > 2-propanol) (Table V). On flushing the hexane with O₂ or N₂, there is no difference in the extent of reaction (Table V) or in the product distribution and the same applies to methanol. The triplet quenchers piperilene and 1,3-cyclohexadiene reduce the reaction rate in hexane but do not lead to significant differences in product ratios. Benzophenone, isobutyrophenone, and 18 at concentrations that absorb >90% of the incident light act as sensitizers in allowing the reaction to proceed and in yielding a modified product mixture even though the overall reaction rate is less than without sensitizer. Acetone also acts as a sensitizer.

Photoproducts Retaining Portions of the Acid and Alcohol Moieties. At early stages of the reaction (<10%

Table III. Photoproducts Detected with Three Labeled Preparations of [¹⁴C]Decamethrin Exposed to Sunlight in Methanol Solution or in the Solid Phase

Labeling position	Irrad. time, h	Yield, %					Low <i>R_f</i>
		Cis ^a	Trans ^b	9	17	18	
Methanol Solution							
¹⁴ C _v	4	77	20	3			0
	8	57	36	5			2
¹⁴ C _N	4	65	27		5		3
	8	66	30		3		1
¹⁴ C _α	4	77	23		0	0	0
	8	56	31		4	9	0
Solid Phase							
¹⁴ C _v	4	9	74	6			11
	8	6	68	9			17
¹⁴ C _N	4	8	70		4		18
	8	2	74		7		17
¹⁴ C _α	4	11	65		7	0	17
	8	7	66		9	0	18

^a Mixture of 2 and 2' as determined by TLC (A × 3, B × 2) as in Table I. ^b Mixture of 3, 3', 4, and 4' in methanol and 3 and 4' in the solid phase as determined by TLC (A × 3 and B × 2) as in Table I.

Table IV. Effect of Solvent and Photosensitizer on Photoproducts Detected with [¹⁴C_α]Decamethrin Exposed to Sunlight

Solvent	Irrad. time, days ^a	Compound, % ^b						Ratio		
		1(1')	2(2')	3(3')	4(4')	18	Low <i>R_f</i>	2(2'):	3(3'):	4(4')
Methanol	2	76.9	13.4 ^c	3.9	3.6	1.6	0.6	3.7:	1.1:	1.0
	8	31.7	28.9	9.0	7.8	9.0	13.6	3.7:	1.2:	1.0
Ethanol	8	49.1	30.1	9.5	8.3	1.2	1.8	3.6:	1.1:	1.0
2-Propanol	8	70.6	11.5	8.5	7.8	1.6	0.0	1.5	1.1:	1.0
Methanol-isobutyrophenone	2	16.0	10.5	28.6	40.7	0.0	4.2	1.0	2.7:	3.9
	8	11.1	7.1	20.7	28.7	0.0	32.4	1.0:	2.9:	4.0

^a Results of single experiment at 2 days exposure and average of two experiments at 8 days exposure. ^b Resolved by TLC (A × 3, B × 2) as in Table I. Corrected for losses of ~5% during TLC analysis. Compounds detected after 2 days exposure in benzene and cyclohexane were 1(1'), 3(3'), and material of low *R_f* in amounts of 83.8, 8.0, and 8.2%, respectively, in benzene and 60.5, 6.0, and 33.5%, respectively, in cyclohexane. ^c Only a portion of the formation of 2 is attributable to photochemical processes. Thus, a comparable (8.0 × 10⁻⁴ M) nonirradiated control reaction gives 8.8% 2. At lower concentration (1.0 × 10⁻⁴ M) there is complete racemization at the α position within 2 days at 25 °C and essentially none at <5 °C.

conversion), most of the photoproducts retain the ester linkage. Compounds identified at 30–50% conversion are quantitated in Table II. Ester cleavage products predominate at >80% conversion.

The trans isomers (3 + 4') are the major photoproducts retaining the ester bond when the irradiations are carried out in aqueous acetonitrile to 30–50% conversion whereas trans products are observed in only minor amounts in methanol and are absent in hexane at similar conversions (Table II). Increases in solvent viscosity lead to increased amounts of products isomerized in the acid moiety as well as unidentified compounds in which the ester linkage is preserved. Thus, in 2-propanol, the trans isomers are observed in 21% yield. Photodecomposition of 1 is sensitized by benzophenone, isobutyrophenone, and 18 to form greater proportions of isomerized material and of unidentified esters.

The major ester photoproducts obtained from 1 in methanol and hexane are the debrominated esters (5 and 6) (Table II). With photolysis in deuterated methanol (CD₃OD), the anticipated monodeuterio products ([²D]5 and [²D]6) are obtained based on GC–MS analyses. Minor amounts of 7 and 8 are formed in methanol or acetonitrile–water but not in hexane.

Photoproducts Derived from the Acid Moiety Only. The cis acid (9) is always the major photoproduct derived from the acid moiety of 1 (Table II). Smaller amounts of the two isomeric debrominated acids (10) are also formed. In methanol and CD₃OD the methyl and trideuteriomethyl esters (11 and [²D₃]11) of 9 are obtained (CI–MS). The

Table V. Relative Extent of Photolysis of Decamethrin in Solutions Irradiated with Ultraviolet Light as Affected by Solvent Viscosity, Quenchers, and Sensitizers

Solvent (viscosity) ^a	Additive	Conversion	
		%	Relative rate
Methanol (0.60)	None	49	3.1
Ethanol (1.2)	None	38	2.4
2-Propanol (2.3)	None	24	1.6
Acetonitrile–water	None	16	1.0
Cyclohexane (1.0)	None	42	1.0
Hexane (0.33)	None	62	1.5
Hexane	O ₂ saturation	62	
Hexane	Piperilene	36	
Hexane	1,3-Cyclohexadiene	24	
Hexane	Benzophenone	22	
Hexane	Isobutyrophenone	42	
Hexane	18	36	
Acetone	None	33	

^a Solvents were flushed with N₂ at –20 °C for 2 h prior to preparation of the solutions. Viscosity in centipoises at 20 °C (except cyclohexane at 17 °C) according to Weast (1969).

methyl esters (12) of the two isomeric debrominated acids (10) are detected in methanol. Minor products from photolysis in methanol are the aldehyde (14) and a compound with a quasimolecular ion cluster (CI–MS) which corresponds to either dibromovinylcyclopropane or its ring-opened isomer (16). The yields in Table II are

Table VI. Mouse Intraperitoneal LD₅₀ Values for Decamethrin, Its Isomers, and Photoproducts

Compound or fraction	LD ₅₀ , mg/kg, with indicated pretreatment		
	Normal	PB	DEF
Authentic Standards			
Designation	Configuration		
1	1 <i>R</i> ,3 <i>R</i> , α <i>S</i>	10	2.9
2	1 <i>R</i> ,3 <i>R</i> , α <i>R</i>	> 500	> 500
1 + 2	1 <i>R</i> ,3 <i>R</i> , α <i>RS</i>	22	6.0
1' + 2'	1 <i>S</i> ,3 <i>S</i> , α <i>RS</i>	> 500	> 500
3 + 4	1 <i>R</i> ,3 <i>S</i> , α <i>RS</i>	> 500	450
3' + 4'	1 <i>S</i> ,3 <i>R</i> , α <i>RS</i>	> 500	> 500
Photodecomposed Decamethrin ^a			
Condition	Fraction		
Solid phase	Hexane ^b	14	
Solid phase	Ether ^c	430	
Acetonitrile-water	Hexane ^b	18	
Acetonitrile-water	Ether ^c	90	

^a LD₅₀ values for individual photoproducts using normal mice are 525 and 350 mg/kg for **9** and **20**, respectively.

^b Consists almost entirely of **1** and its isomerized derivatives (**2-4** and **1'-4'**). ^c Contains no **1** or its isomerized derivatives.

minimal figures for the relatively volatile compounds (**11**, **12**, **14**, **16**) since some loss may occur during workup and isolation.

Photolysis of the acid **9** in methanol yields the corresponding methyl ester (**11**) (47%) and the two isomeric debrominated acids (**10**) (each in 14% yield) and their esters (**12**) (each in 11% yield). When **11** is irradiated in methanol, the debromo esters (**12**) are obtained in equal yields. However, photolysis of **11** in methanol with isobutyrophenone sensitizer (5.0×10^{-2} M) gives a 2:3 mixture of *cis*- and *trans*-methyl esters (**11** and **13**, respectively).

Aldehyde **14** photolyzes in methanol at a rate approximately five times faster than **1**. The products obtained are the acid **9** (40%), ester **11** (11%), and acetal **15** (15–20%). Two photoproducts of **14** are unidentified, one with $[M + 1]^+$ at *m/e* 391 and the other at *m/e* 375. No debrominated products of **14** are detected.

Photoproducts Derived from the Alcohol Moiety Only. The alcohol moiety of **1** yields aldehyde **17** (quantitated along with cyanohydrin **18**) as a major product in all solvents. Cyanohydrin **17** is unstable on GC (upon heating it yields **18**), but it can be analyzed by TLC. The TLC analyses revealed low yields of **17** in methanol and hexane and larger amounts in aqueous acetonitrile. Trace amounts of acetal **19** are obtained in methanol solution. Major photoproducts are 3-phenoxybenzoic acid (**20**) in aqueous acetonitrile, 3-phenoxybenzoyl cyanide (**21**) in hexane, and methyl 3-phenoxybenzoate (**22**) in methanol or trideuteriomethyl 3-phenoxybenzoate ($[^2D_3]22$) in CD₃OD. 3-Phenoxybenzyl nitrile (**23**) is evident in all solvents and in CD₃OD the monodeuterio compound ($[^2D]23$) is formed. Dimers **24-26** arising from the alcohol moiety are detected only in hexane.

Photolysis of cyanohydrin **17** in methanol yields as the sole photoproduct aldehyde **18** which in turn reacts to yield acetal **19** as its major product. The isolated acetal (**19**) on examination by CI-MS gave a small molecular ion peak while the base peak (*m/e* 213) arose from loss of methanol (Table II).

Photolysis of 3-phenoxybenzoyl cyanide (**21**) gives methyl 3-phenoxybenzoate (**22**) in methanol and 3-phenoxybenzoic acid (**20**) in aqueous acetonitrile. These same products are obtained upon heating at 50 °C in the dark. Both **20** and **22** are photostable compounds.

Other Photoproducts. All photolysis mixtures obtained from compound **1** were inspected by TLC with the 4-(*p*-nitrobenzyl)pyridine spray reagent (Hammock et al., 1974) for the possible presence of epoxides, but none were detected.

Comparative Photostability of Related Pyrethroids.

The photodecomposition of **1** was compared to that of NRDC 149 and permethrin in methanol solution (1.0×10^{-3} M, $\lambda > 290$ nm, ~2 days) and in the solid phase (3 mg/cm² on glass, sunlight, 30 h). On photolysis in methanol, only 5% **1** remains while 55% NRDC 149 and 70% permethrin are recovered. In sunlight, 40% **1** reacts and there is no detectable change with either NRDC 149 or permethrin.

Toxicity of Photoproducts. Only the (1*R*, α *S*)-decamethrin isomers show sufficient mouse toxicity for LD₅₀ determinations (Table VI). Thus, only the (1*R*,3*R*, α *S*) isomer (**1**) and the (1*R*,3*S*, α *S*) isomer (**3**, assayed as a mixture with **4**) are of interest relative to their acute toxicity to mammals. Both of these compounds are increased in toxicity by PB and DEF. PB is the most potent synergist for **1**, suggesting that metabolism by oxidases is significant in limiting its toxicity. On a comparable basis, the DEF synergism of **3** indicates that esterases are important in its detoxification. Two of the major photoproducts (**9**, **20**) are of low acute toxicity relative to **1**. The hexane-soluble fraction of photolyzed **1** is slightly less toxic than **1** itself, probably because of some photoisomerization (Table VI). The ether-soluble fraction, lacking any of the decamethrin isomers, is much less toxic.

DISCUSSION

The UV spectrum of **1** in hexane or methanol exhibits a 230-nm band ($\epsilon > 1000$) for the allowed $\pi-\pi^*$ transition of the phenyl rings and a 275-nm band ($\epsilon > 100$), which is essentially $n-\pi^*$ in character, resulting from the combined transitions of the carbonyl system and the lower energy band of the aromatic rings. These $\pi-\pi^*$ and $n-\pi^*$ transitions can lead to the production of either singlet or triplet excited states so no unique excited state can be invoked to explain the variety of photoreactions undergone by the various functional groups of **1**. Incomplete quenching and in some cases inefficient sensitization indicate instead the involvement of reactive states of different multiplicity.

Figures 1 and 2 give the photolysis sequences for **1** under various irradiation conditions. The rate and product distribution depend upon the phase in which the reaction is carried out, the irradiation wavelength and intensity, and the polarity and viscosity of the medium. The identified photoproducts formed upon UV irradiation in solution arise predominantly from ester cleavage reactions, while those formed on sunlight irradiation in the solid phase and in solution in the most part retain the ester linkage intact. The products obtained can be rationalized as originating

from any one of four photochemical processes (A-D).

Process A involves cyclopropane ring opening and various recombinations (cis/trans isomerization to yield 2', 3, and 4') or fragmentation (to form 7) (Bullivant and Pattenden, 1971; Elliott and Janes, 1973; Holmstead et al., 1977; Sasaki et al., 1970; Ueda and Matsui, 1971). A triplet excited state is involved in process A since sensitization with isobutyrophenone ($E_t = 73$ kcal/mol) results in cis/trans isomerization as the major reaction of 1 and 11 (to yield 13) at the initial stage. Triplet quenchers such as piperilene ($E_t = 53$ kcal/mol) and 1,3-cyclohexadiene ($E_t = 50$ kcal/mol) are effective in decreasing the extent of reaction. Unidentified, polar photoproducts are also formed on sensitization. In the absence of sensitizer, process A predominates, regardless of the irradiation source, in the solid phase and in a viscous solvent (i.e., 2-propanol) as opposed to ones of lower viscosity (i.e., methanol and ethanol).

Process B, involving scission of the ester oxygen-benzyl carbon bond, is an important reaction in both solution and the solid phase. The radicals in a solvent cage process either regenerate 1 or the alcohol fragment racemizes prior to recombination, forming 2 as observed upon sunlight irradiation. In general, racemization is anticipated in such reactions. An alternative mechanism for racemization in the alcohol moiety would involve abstraction of the α -methylene proton by the carbonyl diradical to yield a benzylic radical which can isomerize, followed by back-abstraction of the same proton by intramolecular transfer. However, several observations rule against this hypothesis. First, 2 is not detected in the solid phase where this process should be favored. Second, solvent polarity has a marked effect on the rates of carboxyl-carbon bond cleavage and recombination, indicating that the solvent interacts with the excited state. Third, intramolecular proton abstraction in esters usually involves a six-membered transition state (Bartrop and Coyle, 1971; Coyle and Kingston, 1976) rather than the five-membered intermediate in this hypothesis.

At UV wavelengths there is negligible recombination of the radicals (i.e., ester cleavage products predominate). This implies that the radicals diffuse rapidly from the cage or that they recombine in a stereospecific manner similar to observations on other compounds (Finnegan and Knutson, 1967; Givens and Matuszewski, 1975). The ratio of ester products from isomerization at the cyclopropane ring to those from racemization at the α position is increased on changing from methanol or ethanol to 2-propanol and particularly on sensitization as anticipated from results on sensitization of other pyrethroids (Bullivant and Pattenden, 1971; Ueda and Matsui, 1971). Thus, the primary cis product is likely to be 2' with sensitizer and 2 in the absence of sensitizer, only the former reaction proceeding via a triplet excited state. Formation of the α -R epimer 2 appears to result largely from a ground-state reaction in which the α proton exchanges with the solvent. Accordingly, the yields obtained for this isomer must be viewed with caution since they do not represent purely photochemical processes.

On irradiation with UV light, 2 is not detected and process B leads instead to formation of carboxyl and benzyl radicals which upon hydrogen abstraction yield 9 and 23. The benzyl radicals also dimerize in hexane to 24-26. A minor product (8) results from carbon dioxide elimination, followed by radical recombination (Givens and Oettle, 1972; Matuszewski et al., 1973); larger amounts of analogous decarboxylated materials are formed from some other α -cyano esters, including pyrethroids (Holmstead

and Fullmer, 1977; Holmstead et al., 1977). Decarboxylation in other systems occurs via radical intermediates, and in some cases "cage" effects are postulated (Jaeger, 1975). Dibromovinyl acid 9 produced in pathway B reacts to yield 11 in methanol, as confirmed by direct irradiation of 9 and by analogy with findings on other compounds (Barbieri et al., 1969).

Process C, reductive debromination, is an important photoreaction of 1, 9, and 11 at UV wavelengths. The major pathway for formation of 10 and 12 from 1 probably proceeds via 5 and 6, i.e., debromination before ester cleavage, since at early stages in the photolysis most of the radiation is absorbed by the intact esters. Both ionic (electron transfer) and free radical mechanisms have been suggested (McNeely and Kropp, 1976; Suzuki et al., 1976) for the carbon-halogen bond cleavage in vinyl halides and haloalkenes in general. Ionic cleavage yields products arising from nucleophilic attack by the solvent, while free radical intermediates abstract hydrogen from the solvent. Only the latter process was observed in photolysis of 1; however, it is possible that products containing oxygen at the vinyl position are unstable and are not detected. In this study, trans debromination leading to 5 is preferred (4:1) over cis debromination to 6 on photolysis in methanol; the same preference (4:1) is observed using triphenyltin hydride which proceeds by abstraction of a bromine atom to yield a vinyl radical. The greater photochemical yield of the trans-debromo product 5 must be caused by steric effects from the alcohol moiety of 1 since the methyl ester 11 exhibits no such preference for trans debromination yielding the isomers of 12 in equal amounts upon photolysis or treatment with triphenyltin hydride. Inspection of Dreiding models of 1 shows that the *trans*-bromine substituent is not shielded by the diphenyl ether group, thus the bromine atom produced upon bond cleavage at the *trans* position can drift apart with greater ease than that at the *cis* position, especially since the latter may be complexed with the π system of the aromatic rings, in a manner similar to that postulated for chlorine atoms with aromatics (Fox et al., 1973).

Ester cleavage products can also arise by process D involving scission of the acyl-oxygen bond (Breslow and Baldwin, 1970). This process yields 14 from the acid moiety and 17 and 21 from the alcohol moiety. The carbonyl radical in process D may undergo decarbonylation to form 16 or this product may arise via hydrogen abstraction by the radical formed in process B on decarboxylation of 1 (Finnegan and Knutson, 1967; Simonaitis and Pitts, 1969). The dibromovinyl acids and methyl esters may also form by further reaction of the aldehyde 14 with the solvent or by photooxidation; no debrominated products are observed in the photolysis of 14. In methanol, aldehyde 14 yields acetal 15. The route for formation of aldehyde 18 is suggested by the conversion of cyanohydrin 17 readily to 18 in solvent or in the solid phase. The aldehyde photoproduct 18 sensitizes the photodegradation of 1. The major ester cleavage products (20, 22) may result from nucleophilic attack of the solvent on 21, since 21 in aqueous or methanolic solution yields 20 and 22 upon photolysis or on heating. Benzoyl cyanide 21 is detected as a prominent product only in hexane. The aldehyde in methanol yields 19.

Permethrin and NRDC 149 in methanol or hexane show essentially the same UV spectra as 1, thus the greater reactivity of 1 must be the result of its chemical composition (dibromovinyl and cyano substituents) and not of its absorption characteristics. Lower bond strengths, steric effects, and increased population rates (intersystem

crossing) are probably important factors contributing to the photolability of 1.

The photoproducts of 1 are less toxic on an acute basis to mice than 1 itself. This includes the individual esters resulting from isomerization in the acid moiety and racemization in the alcohol moiety and the overall mixture of photoproducts. Thus, as far as acute toxicity is concerned, the amount of 1 is of greater toxicological significance than that of any of its photoproducts.

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Toxaphene Components and Related Compounds: Preparation and Toxicity of Some Hepta-, Octa-, and Nonachlorobornanes, Hexa- and Heptachlorobornenes, and a Hexachlorobornadiene

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Five major toxaphene components [2,2,5-*endo*,6-*exo*,8,9,10-heptachlorobornane (B) and its 3-*exo*-chloro, 8-chloro, 9-chloro, and 10-chloro derivatives] collectively account for up to 23% of the GLC-electron-capture properties of chlorinated technical grade camphene (i.e., toxaphene insecticide) and up to 34% of those of chlorinated 2-*exo*,10-dichlorobornane. Chlorination of 2-*exo*,10-dichlorobornane provides a convenient source of B, which on further chlorination gives the indicated octachlorobornanes and the 5-*exo*-chloro derivative of B plus two nonachlorobornanes, one with the introduced chlorines at C-8 and C-10 and the other with these chlorines at the 3-*exo* position and at C-10. On dehydrochlorination B yields two hexachlorobornenes and the 3-*exo*-chloro derivative of B gives one heptachlorobornene and one hexachlorobornadiene. The toxicity to mice, houseflies, and goldfish of the octachlorobornanes formed by introducing chlorine substituents into B, relative to B itself, generally decreases in the order: 9-chloro > 8-chloro > no added chlorine (i.e., B) > 3-*exo*-chloro, 5-*exo*-chloro, or 10-chloro.

The amount of toxaphene used in the United States continues to be larger than that of any other insecticide. It is therefore essential to define the composition of

toxaphene and the toxicological properties of its components.

Toxaphene is produced by chlorination of camphene to yield a very complex mixture with an overall composition approximating C₁₀H₁₀Cl₈. Two of its most toxic components are 2,2,5-*endo*,6-*exo*,8,9,10-heptachlorobornane (compound B) and a mixture of the 8-chloro and 9-chloro derivatives of B (referred to here as 8-Cl-B and 9-Cl-B,

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