Photodecomposition of Resmethrin and Related Pyrethroids

Kenzo Ueda, Loretta C. Gaughan, and John E. Casida*

Photodecomposition of resmethrin on various surfaces or in water yields the following products: nonisomerized chrysanthemic acid, phenylacetic acid, benzyl alcohol, benzaldehyde, and benzoic acid from cleavage reactions; the chrysanthemates of 5-hydroxy-3-oxo-4-phenyl-1-cyclopentenylmethanol, 2-benzyloxy-5-oxo-2,5-dihydro-3-furylmethanol, and 5-benzyl-5-hydroxy-2-oxo-2,5-dihydro-3-furylmethanol; the isomeric epoxychrysanthemates with the alcohol moiety unmodified or with the first alcohol mentioned above; and many unidentified photoproducts, mostly esters. The ester photoproducts oxidized in the alcohol moiety probably originate from a cyclic peroxide. (+)-*trans*-Chrysanthemic acid is more toxic than resmethrin on intraperitoneal administration to mice. Photoepoxidation reduces the toxicity of resmethrin and some other chrysanthemates and ethanochrysanthemates to houseflies. The unpleasant odor of photodecomposed resmethrin is due, in part, to phenylacetic acid. Structural features limiting the persistence of resmethrin and related pyrethroids include the easily epoxidized isobutenyl and cyclopentylidenemethyl groups, the photolytically labile ester group, and, particularly, the photosensitive furan ring.

Pyrethrum and many synthetic pyrethroids are effective insect control agents but the scope of their use is limited by high cost and photoinstability. There has been some success in prolonging the persistence of pyrethroids by modifying their chemical structure and by adding antioxidants, photoscreens, and other materials to retard their degradation in light and air (Abe *et al.*, 1972; Chen and Casida, 1969; Miskus and Andrews, 1972). The photodecomposition products of the chrysanthemate moiety of pyrethrin I, allethrin, tetramethrin, and dimethrin (Chen and Casida, 1969) and of the alcohol moiety of allethrin (Elliott and Janes, 1973) are partially defined. An understanding of the photodecomposition process is important in solving instability problems and developing more stable pyrethroids.

Resmethrin and its alcohol moiety photodecompose to many unidentified products at a rate which varies with the supporting surface (Rosen, 1972). The present study considers the identity and amounts of the resmethrin photoproducts as affected by the photodecomposition conditions. It also includes some comparative investigations with other pyrethroids.

MATERIALS AND METHODS

Spectroscopy. The following instrumentation was used for spectroscopic studies: Perkin-Elmer Model 457 grating infrared (ir) spectrophotometer; type 21-103C mass spectrometer (Consolidated Electrodynamic Corp., Pasadena, Calif.) operated at 170° and 70 eV for mass spectra by electron impact; Finnigan 1015D mass spectrometer with a chemical ionization (CI) source using methane at 1000 μ pressure as the reactant gas; Perkin-Elmer Model R12B nuclear magnetic resonance (nmr) spectrometer. The nmr shift reagent used was tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione)europium(III)-d_{30} referred to here as Eu(fod)$_3$ (Norell Chemical Co., Inc., Landing, N. J.). Chemical shifts (δ) are reported in parts per million downfield from tetramethylsilane and coupling constants (J) are expressed in hertz.

Chromatography. Thin-layer chromatography (tlc) utilized precoated 20 × 20 cm chromatoplates as follows: silica gel 60 F-254 (with fluorescent indicator) or silica gel 60 (without fluorescent indicator) with 0.25-mm gel thickness (EM Laboratories, Inc., Elmsford, N. Y.) for analytical studies; silica gel GF with 1.0-mm gel thickness (Analtech, Inc., Newark, Del.) for preparative isolations. Eleven tlc solvent systems were used: (A) *n*-hexane–ether (5:1); (B) *n*-hexane–ether (1:1); (C) ether–*n*-hexane (2:1); (D) carbon tetrachloride–ether–*n*-hexane (8:1:1); (E) chloroform–ether–*n*-hexane (8:1:1); (F) chloroform–acetonitrile–*n*-hexane (8:1:1); (G) benzene–ether–*n*-hexane (1:1:1); (H) benzene–ethyl acetate–methanol (15:5:1); (I) benzene–ethyl acetate–methanol (5:5:1); (J) chloroform–ether–acetic acid (10:3:1); (K) benzene saturated with formic acid–ether (10:3). Two combinations of developments were used for two-dimensional tlc; procedure X refers to two consecutive developments in the first direction with solvent system A and then one development with solvent system F in the second direction; procedure Y refers to two developments with solvent system F in the first direction, then one development with solvent system C, and then a second with solvent system K in the second direction. Procedure X, involving a rather nonpolar solvent combination, resolves relatively nonpolar compounds while procedure Y, a more polar combination, separates the polar photoproducts. The following methods were used for detection of resolved products: quenching of gel fluorescence when viewed under short-wavelength uv light; spraying with 20% (w/v) phosphomolybdic acid in ethanol followed by heating at 115° for 5 min; spraying with 5% (w/v) 4-(*p*-nitrobenzyl)pyridine in acetone followed by heating for 16 min at 150° and then overspraying with 10% (w/v) tetraethylenepentamine in acetone at 25° to yield blue to bluish-purple spots on a white background with high specificity and sensitivity (1–10 μg) for several types of epoxides (Hammock, 1973). Radioactive gel regions detected by radioautography were scraped free from the glass support into scintillation vials for liquid scintillation counting (lsc).

For column chromatography, a homogeneous mixture of 200 g of silicic acid (100 mesh, Mallinckrodt) and 90 ml of water was slurried in *n*-hexane to prepare a 32-cm column of 4 cm i.d. This column was developed with 300 ml each of *n*-hexane, various ether in hexane mixtures (v/v, per cent) (5, 10, 15, 20, 30, 40, 60, and 80), followed by ether (1 l.). Each fraction (10 ml) was examined by tlc and fractions of similar composition were combined.

Gas–liquid chromatography (glc) utilized glass columns (1.8 m × 3.2 mm i.d.) containing 3% SE-30 or 10% DC-200 on Gas-Chrom Q (80–100 mesh) and 5% diethylene glycol adipate on Chromosorb WHP (80–100 mesh) in each case with a nitrogen flow rate of 20 ml/min and a flame ionization detector.

Chemicals. [^{14}C]*Pyrethroids.* Various samples of isomerically and optically pure [^{14}C]resmethrin, -tetramethrin, and -allethrin, each of greater than 99% radiochemical

Division of Entomology and Parasitology, University of California, Berkeley, California 94720.

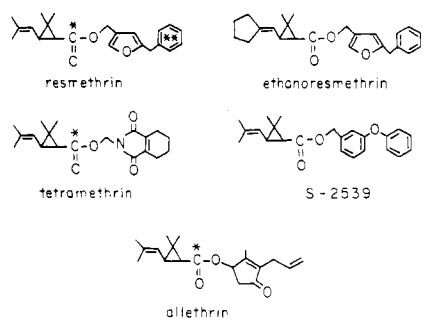

Figure 1. Structures of the five pyrethroids studied. The positions of radiolabeling are indicated as follows: (*) for acid moiety; (**) for alcohol moiety. The isomers used for each study are indicated in the text.

purity, were utilized (Figure 1). The (+)- and (−)-isomer preparations were used interchangeably in different photochemical experiments with resmethrin and tetramethrin because no difference is expected with these antipodes and in fact none was observed on comparing (+)- and (−)-*trans*-resmethrin. *trans*- and *cis*-[1-^{14}C]chrysanthemic acid prepared by a described procedure (Nishizawa and Casida, 1965) were each resolved with (+)- and (−)-α-(*p*-chlorobenzyl)benzylamine to obtain the optically pure isomers of [1-^{14}C]chrysanthemic acid. Conversion of these acids to the acid chlorides and esterification with 5-benzyl-3-furylmethanol (BFA) gave the optically pure isomers of acid-labeled (^{14}C) resmethrin. Alcohol-labeled (^{14}C) (+)-*trans*- and (+)-*cis*-resmethrin were prepared by esterification of the acid chlorides of (+)-*trans*- and (+)-*cis*-chrysanthemic acids with [^{14}C]phenyl-BFA, which was synthesized by the Friedel–Crafts reaction of methyl 5-chloromethyl-3-furoate (Elliott *et al.*, 1971) with equimolar [^{14}C]benzene in the presence of aluminum chloride in nitrobenzene followed by reduction with lithium aluminum hydride. Acid-labeled tetramethrin and allethrin were prepared from the appropriate [^{14}C]chrysanthemic acid isomers by the general procedure described by Abernathy *et al.* (1973).

Unlabeled Pyrethroids and Cleavage Products. The pyrethroids used (Figure 1) are described by Abernathy *et al.* (1973). In order to define the configurational relationships between the original esters and their photodecomposition products, the letters t and c for the trans and cis acid moieties, respectively, are used after the Roman numerals designating the compounds. The name *S*-bioallethrin refers to (+)-allethronyl (+)-*trans*-chrysanthemate. The following nine compounds which can potentially be derived from cleavage of resmethrin with or without subsequent oxidation were also utilized: each of the four isomers of chrysanthemic acid (CA); *trans,trans*-chrysanthemum dicarboxylic acid; BFA; 5-benzyl-3-furoic acid (BFCA); the benzyl alcohol [α-(4-carboxy-2-furyl)benzyl alcohol] and keto derivatives (5-benzoyl-3-furoic acid) of BFCA referred to as α-OH-BFCA and α-keto-BFCA, respectively.

Esters of Epoxychrysanthemic Acids. Epoxidation of the pyrethroid with equimolar *m*-chloroperoxybenzoic acid in dichloromethane at 25° gave in good yield a mixture of the two isomeric epoxy esters usually separable by tlc. After filtration, solvent evaporation, addition of ether, and washing the ether with 5% sodium carbonate solution, the epoxy esters in the ether were isolated by preparative tlc. The R_f values reported are for two developments with solvent system A using fluorescent tlc chromatoplates. The mass spectral data are those obtained with the CI source. The configurational assignments of the epoxy esters are based on nmr: the 1*R*,3*S*,1′*R* isomer and its enantiomer are referred to as the *R* isomer; the 1*R*,3*S*,1′*S* isomer and its enantiomer are referred to as the *S* isomer. The (1*R*,3*S*,1′*R*)- and (1*R*,3*S*,1′*S*)-epoxide isomers are derived from esters of (1*R*,3*R*)-*trans*-chrysanthemic acid, the change of symbol at position 3 being a consequence of the definition of preferences by the sequence rule. For this consideration, H_1, H_3, and $H_{1'}$ are used to designate the protons attached to C_1 adjacent to the carbonyl group, C_3 adjacent to the unsaturated side chain, and $C_{1'}$ of the side chain. The spectroscopic data for the structural assignments are given below.

(+)-*trans-Epoxyresmethrin.* Preparative tlc using two developments with solvent system A yielded the *R* isomer (R_f 0.24; n^{22}D 1.5208) and the *S* isomer (R_f 0.32; n^{22}D 1.5168). Neither compound showed ir absorption due to hydroxyl groups. The mass spectral (CI) data are essentially the same for the two isomers: *m/e* (rel intensity) 395 (<1) (M + 41), 383 (<1) (M + 29), 355 (2) (M + 1), 353 (1) (M − 1), 337 (4) (M − 17, which is M + 1 − H_2O characteristic of an epoxide), 325 (2), 297 (2–3), 277 (1), 211 (3–4), 199 (8–9), 171 (100) (due to alcohol fragment), 167 (7–10), 139 (5–7) (due to acid fragment), 123 (12–16). The nmr spectra differ for the two isomers: for the *R* isomer (CCl_4) δ 1.20 (3 H, s), 1.22 (3 H, s), 1.27 (6 H, s), 3.87 (2 H, s), 4.83 (2 H, s), 5.95 (1 H, s), 7.17 (5 H, s), 7.28 (1 H, s), H_1 1.43 (1 H, d, J = 5.5 Hz), H_3 1.2 and $H_{1'}$ 2.31 ppm (1 H, d, J = 7.5 Hz); for the *S* isomer (CCl_4) δ 1.18 (9 H, s), 1.23 (3 H, s), 3.87 (2 H, s), 4.82 (2 H, s), 5.94 (1 H, s), 7.16 (5 H, s), 7.25 (1 H, s), H_1 and H_3 1.52 (2 H, m) and $H_{1'}$ 2.57 ppm (1 H, d, J = 2 Hz). The coupling constants between H_3 and $H_{1'}$ are greatly different for the two isomers. Examination of Dreiding molecular models indicates that a dihedral angle of close to 90° between H_3 and $H_{1'}$ is more favorable in the *S* isomer than in the *R* isomer since there is enhanced steric repulsion between the two residual groups attached to C_3 and $C_{1'}$ in one of the 90° conformers of the *R* isomer, but no such repulsion occurs in either of the 90° conformers of the *S* isomer. Therefore, the coupling constant between these hydrogens would be expected to be smaller in the *S* than in the *R* isomer. In (+)-cis isomers, however, no such favorable condition exists for a dihedral angle of 90° between H_3 and $H_{1'}$, even in the *S* isomer, since the residual group attached to $C_{1'}$ is very near to the large alkoxycarbonyl moiety in the (+)-cis isomers instead of to the small H_1 hydrogen in the (+)-trans isomers, so the *R* and *S* isomers of the cis compound each give the same large coupling constant of 6.8 Hz. The higher chemical shift of the $H_{1'}$ proton in the *R* isomer may be explained by the anisotropy of the cyclopropane ring, since the H_1 proton in the *R* isomer more easily assumes the position right under the plane of the cyclopropane than in the *S* isomer.

(+)-*trans-Epoxyethanoresmethrin.* Two tlc developments with solvent system A yielded the isomeric products, identified as the *R* isomer (R_f 0.35; n^{22}D 1.5280) and the *S* isomer (R_f 0.40; n^{22}D 1.5280). The mass spectra (CI) are essentially the same for the two isomers: *m/e* (rel intensity) 421 (<1) (M + 41), 409 (<1) (M + 29), 381 (6) (M + 1), 379 (1–2) (M − 1), 363 (8–11) (M − 17), 351 (2–3), 201 (4), 199 (6–8), 193 (12–14), 171 (100), 165 (3–4), 149 (9–16). The nmr spectra differ for the two isomers: for the *R* isomer (CCl_4) δ 1.19 (3 H, s), 1.27 (3 H, s), 1.71 (8 H, br m), 3.87 (2 H, s), 4.84 (2 H, s), 5.95 (1 H, s), 7.17 (5 H, s), 7.28 (1 H, s), H_1 1.43 (1 H, d, J = 5.5 Hz), H_3 1.17 and $H_{1'}$ 2.53 ppm (1 H, d, J = 8.3 Hz, decoupled to a singlet by irradiation at δ 1.17); for the *S* isomer (CCl_4) δ 1.21 (6 H, s), 1.68 (8 H, br m), 3.89 (2 H, s), 4.84 (2 H, s), 5.96 (1 H, s), 7.19 (5 H, s), 7.28 (1 H, s), H_1 and H_3 1.48 (2 H, s) and $H_{1'}$ 2.88 ppm (1 H, s).

(+)-*trans-Epoxy-S-2539.* Following separation with solvent system D, the *R* and *S* isomers (R_f 0.25 and 0.35, respectively) are differentiated by nmr as follows: for the *R* isomer (CCl_4) δ 1.22 (3 H, s), 1.25 (3 H, s), 1.30 (6 H, s), 5.03 (2 H, s), 6.7–7.5 (9 H, m), H_1 1.47 (1 H, d, J = 6 Hz), H_3 1.2 and $H_{1'}$ 2.32 ppm (1 H, d, J = 7.5 Hz, decoupled to a singlet by irradiation at δ 1.2); for the *S* isomer

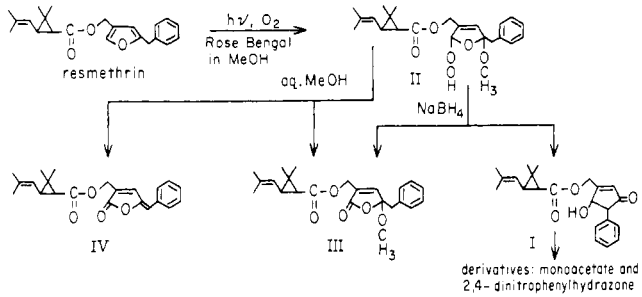

Figure 2. Photosensitized oxidation of (+)-*cis*-resmethrin and formation of derivatives from the methoxy hydroperoxide photoproduct. The chemical names of compounds designated by Roman numerals are given in the text where they are referred to as I-c, II-c, III-c, and IV-c since they are derived from *cis*-resmethrin.

(CCl_4) δ 1.21 (9 H, s), 1.24 (3 H, s), 5.01 (2 H, s), 6.7-7.5 (9 H, m), H_1 1.60 (1 H, d, J = 5.5 Hz), H_3 1.52 (1 H, d of d, J = 2.5, 5.5 Hz), and $H_{1'}$ 2.60 ppm (1 H, d, J = 2.5 Hz, decoupled to a singlet by irradiation at δ 1.52).

(±)-*trans-Epoxytetramethrin.* The individual isomeric epoxy esters were not separated on preliminary tlc purification with solvent system H nor were they resolved with solvent system F, but two spots were obtained on developing twice in the same direction first with solvent system C and then with solvent system K. The presence of two isomeric epoxy esters in the oil was confirmed by nmr which showed characteristic proton signals at δ 2.70 (d, J = 3 Hz) and 2.52 (d, J = 7 Hz) in $CDCl_3$, which gave a one-proton integration in total. One of the latter signals was obscured by methylene signals, but its doublet character was clearly established by addition of the shift reagent, Eu(fod)$_3$. The doublet signals at δ 2.70 and 2.52 were decoupled to singlets by irradiation at δ 1.57 and 1.42, respectively. Other nmr signals were in accord with the proposed structure; mass spectrum (CI) m/e (rel intensity) 348 (<1) (M + 1), 330 (<1) (M − 17), 167 (25), 164 (59) (alkyl fragment of alcohol moiety), 139 (6) (alkyl fragment of acid moiety), 123 (63), 73 (100), 61 (95). 3,4,5,6-Tetrahydrophthalimidomethyl acetate was not epoxidized under this condition so epoxidation in the alcohol moiety of tetramethrin is not involved.

(+)-*cis-Epoxy Derivatives of Resmethrin, Ethanoresmethrin, and S-2539.* These compounds were prepared from the corresponding (+)-*cis*-pyrethroids and isolated and identified by the general procedures given above. The configuration of each isomer was not individually assigned.

5-Hydroxy-3-oxo-4-phenyl-1-cyclopentenylmethyl trans-2',3'-Epoxychrysanthemate (VII-t, the Epoxide of I-t). The parent ester I-t (Figure 6, described later) was epoxidized and purified by tlc with solvent system H. The nmr spectrum of the product in comparison with the original ester showed: two additional doublets, which gave a combined integration comparable to one proton, at δ 2.74 (J = 3.5 Hz) and 2.57 (J = 8.5 Hz) in $CDCl_3$, the latter doublet about half of the former in their integration; loss of the doublet at δ 4.86 due to the olefinic proton of the acid moiety; other signals quite similar to those of the original ester. On sequential tlc development with solvent systems C and then K in the same direction, two products were resolved at R_f 0.28 and 0.24 in this solvent system. The upper product, clearly darker with the epoxide spray reagent than the lower one, was assigned as the S isomer; mass spectrum (CI) m/e (rel intensity) 399 (<1) (M + 29), 371 (<1) (M + 1), 353 (<1) (M + 1 − H_2O), 335 (<1) (M + 1 − $2H_2O$), 187 (8) (alkyl fragment of alcohol moiety), 167 (15), 149 (44), 139 (56) (alkyl fragment of acid moiety), 121 (100), 109 (86).

Photosensitized Oxidation of (+)-cis-Resmethrin. Rose Bengal sensitized photooxidation followed by various chemical reactions produced a series of esters oxidized in the alcohol moiety (Figure 2). One of these esters, the cyclopentenolone (I-c), was also isolated from the photoproducts formed on exposure of *cis*-resmethrin deposits to light and air and another one, the methoxy lactone (III-c), is closely related to the hydroxy lactone (V-c) from normal photodecomposition of *cis*-resmethrin.

A mixture of (+)-*cis*-resmethrin (2.0 g) and Rose Bengal (0.1 g) in methanol (600 ml) was irradiated with a 40-W G.E. showcase lamp (General Electric Co., Cleveland, Ohio) for 3 hr while oxygen was bubbled through the solution. Evaporating the methanol, dissolving the residue in ether, washing the ether with water, treating it with activated charcoal (0.5 g), drying (sodium sulfate), and evaporating gave in almost quantitative yield a light yellow liquid. This crude material was essentially a single compound as determined by nmr; tlc analysis with solvent system B on nonfluorescent plates revealed only one major product, R_f 0.49, and trace amounts of resmethrin and a few other compounds. This material readily liberated iodine from potassium iodide solution. Nmr and ir spectra clearly supported the structure, 5-benzyl-2-hydroperoxy-5-methoxy-2,5-dihydro-3-furylmethyl *cis*-chrysanthemate (II-c, Figure 2), as expected from earlier work on related compounds (Foote *et al.*, 1967): nmr ($CDCl_3$) δ 1.23 (6 H, s), 1.68 (6 H, br s), 1.63 (1 H), 1.94 (1 H), 3.05 (2 H, s), 3.23 (3 H, s), 4.50 (2 H, br s), 5.28 (1 H, d, J = 8 Hz), 5.52 (1 H, fine m), 5.77 (1 H, fine m), and 7.12 ppm (5 H, s); ir (direct) 3300 (OOH) and 1726 cm^{-1} (ester C=O).

The positions of the hydroperoxy and methoxy groups were tentatively assigned based on the structures of derived compounds. Compound II-c was reduced with equimolar sodium borohydride in methanol yielding one major product, possibly the 2-hydroxy-5-methoxy derivative, which had a slightly lower tlc R_f than the parent compound in solvent systems B, C, D, and E. Preparative tlc of the crude material with solvent system C resulted in decomposition to give two compounds, 5-hydroxy-3-oxo-4-phenyl-1-cyclopentenylmethyl *cis*-chrysanthemate (I-c) as a major product and 5-benzyl-5-methoxy-2-oxo-2,5-dihydro-3-furylmethyl *cis*-chrysanthemate (III-c) as a minor product. When compound II-c was held in aqueous methanol at 25° for 2 days, compound III-c and 5-benzylidene-2-oxo-2,5-dihydro-3-furylmethyl *cis*-chrysanthemate (IV-c) were formed along with some unidentified compounds.

Compound I-c had the following characteristics: mp 113-115° (*n*-hexane-carbon tetrachloride); mass spectra (70 eV) molecular ion of 354 along with a base peak at 123 for the alkyl fragment of the acid moiety, which is typical of chrysanthemates; uv max (C_2H_5OH) 233 (ϵ 7.12 × 10^3) and 324 mμ (ϵ 110); nmr ($CDCl_3$) δ 1.23 (6 H, s), 1.68 (3 H, d, J = 2 Hz), 1.72 (3 H, d, J = 2 Hz), 1.73 (1 H, d, J = 8 Hz), 1.97 (1 H, d of d, J = 8, 8 Hz), 3.27 (1 H, br, disappeared on addition of D_2O), 3.47 (1 H, d, J = 3 Hz, decoupled to a singlet by irradiation at δ 4.78), 4.78 (1 H, fine m), 5.00 (2 H, s), 5.30 (1 H, d, J = 8 Hz), 6.13 (1 H, fine m), and 6.97-7.42 ppm (5 H, m); ir (nujol) 3410 (OH), 1720 (ester C=O), 1685 and 1675 (α,β-unsaturated C=O), and 1628 cm^{-1} (C=C). *Anal.* Calcd for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.39; H, 7.45.

The acetate of compound I-c was obtained in good yield by acetylation with acetyl chloride and pyridine in benzene. The acetate showed no ir hydroxyl absorption and gave a mass spectral (70 eV) molecular ion at 396, and the nmr spectrum ($CDCl_3$) showed a significant low-field shift of 1.91 ppm to δ 5.97 attributable to the hydrogen on the hydroxyl-bearing carbon without significant change in other signals except for the appearance of one acetyl methyl signal at δ 2.08.

The nmr spectrum of compound I-c suggested that no structural modification occurred in the acid moiety and the phenyl group, but the phenyl group was affected by strong anisotropic effects from other parts of the molecule

to give a multiplet pattern. The uv spectrum suggested that the carbonyl group was conjugated with one double bond but not with the phenyl group. The signal at δ 4.78 in $CDCl_3$ was further examined using dimethyl-d_6 sulfoxide as the solvent; this signal was enhanced twofold in its width and showed a clear doublet of J = 6 Hz on irradiation of the proton at δ 3.47 ($CDCl_3$). This finding and the acetate formation data suggested the existence of only one secondary hydroxyl group. The shift reagent, Eu(fod)$_3$, gave the following effects: the biggest shift of 0.68 ppm due to the proton on the carbon bearing the phenyl group, originally situated at δ 3.47, and the next to largest shift of 0.47 ppm due to the proton at δ 4.78 on the carbon bearing the hydroxyl group. These magnitudes do not take into account any effects on the hydroxyl proton. These findings support the trans configuration of the hydroxyl and phenyl groups.

The 2,4-dinitrophenylhydrazone of compound I-c as the monohydrate (mp 146–147° from carbon tetrachloride–ethyl acetate) gave appropriate elemental analyses and nmr and ir spectra.

Compound III-c had the following characteristics: mp 120–122.5° (*n*-hexane); mass spectra (70 eV) *m/e* (rel intensity) 384 (5) (M^+), 218 (24), 186 (10), 167 (9), 151 (31), 123 (100), 122 (69), 107 (50), 91 (81), 81 (55); nmr ($CDCl_3$) δ 1.22 (6 H, s), 1.63 (1 H), 1.66 (3 H, d, J = 2 Hz), 1.70 (3 H, d, J = 2 Hz), 1.92 (1 H), 3.20 (5 H, s), 4.69 (2 H), 5.30 (1 H, d, J = 7.5 Hz), 6.79 (1 H, fine m), and 7.23 ppm (5 H, s); ir (nujol) 1770 (α,β-unsaturated γ-lactone), and 1724 cm^{-1} (ester C=O). *Anal.* Calcd for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 71.38; H, 7.30.

Compound IV-c had the following characteristics: mp 124–126° (*n*-hexane–carbon tetrachloride); mass spectra (70 eV) *m/e* (rel intensity) 352 (17) (M^+), 186 (73), 185 (93), 167 (88), 157 (80), 129 (93), 128 (85), 127 (82), 124 (75), 123 (100), 122 (81), 121 (85), 118 (58), 115 (63), 107 (85), 95 (68), 93 (63), 91 (81), 90 (83), 81 (98), 77 (69), 67 (85), 57 (60), 55 (90), 53 (74); uv max (C_2H_5OH) 224 (ϵ 1.5 $\times 10^4$) and 336 mμ (ϵ 3.31 $\times 10^4$) supported the conjugated system; nmr ($CDCl_3$) δ 1.20 (3 H, s), 1.24 (3 H, s), 1.65 (3 H, fine d), 1.71 (3 H, fine d), 1.60 (1 H, d), 1.93 (1 H, t, J = 8 Hz), 4.83 (2 H, s), 5.88 (1 H, s), 7.09–7.33 (4 H, m), and 7.5–7.7 ppm (2 H, m); ir (nujol) 1745 (α,β-unsaturated γ-lactone), 1727 (ester C=O), and 1640 cm^{-1} (C=C). *Anal.* Calcd for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 75.00; H, 6.88.

Photodecomposition Procedures. *Unlabeled Resmethrin.* (+)-*trans*-Resmethrin (4.0 g) of (+)-*cis*-resmethrin (3.0 g) was applied at 1.7 mg/cm^2 to silica gel 60 chromatoplates which were then exposed to bright sunlight for 10 hr. The gel was recovered and washed with ether, the solvent evaporated, and the residual oil (about 80% by weight recovery) was fractionated on a silicic acid column. Fractions of similar composition (tlc monitoring) were combined for further purification by preparative tlc with solvent systems D, E, and/or K. The compounds isolated and identified from (+)-*trans*-resmethrin were used as authentic unlabeled standards in the study of *trans*-[^{14}C]resmethrin photoproducts described below. In another experiment, (+)-*trans*-resmethrin was exposed to sunlight by the same procedure for various periods of time; then the ether-soluble material was utilized for mouse toxicity tests and quantitative glc analysis of resmethrin (retention time (T_r) 4.5 min on 3% SE-30 at 230° using di-*n*-octyl phthalate, T_r 6.8 min, as the internal standard) and CA (T_r 4.7 min on 5% diethylene glycol adipate at 175° with dimethyl phthalate, T_r 9.3 min, as the internal standard).

[^{14}C]*Pyrethroids.* The labeled pyrethroid was applied in two 5-μl aliquots of hexane to three types of surfaces (silica gel 60 chromatoplate, Whatman qualitative No. 1 filter paper, or glass) yielding deposits of 10–17 μg/cm^2. As an alternative, the [^{14}C]pyrethroid was dissolved in water (40 ml) at 0.16 ppm in a petri dish (14 cm i.d.) and covered with a quartz plate. The treated surfaces or solution was irradiated with a 275-W G.E. sunlamp at a distance of 30 cm or with sunlight for various time periods. The temperature of the chromatoplates (and probably of the other surface residues) irradiated with the sunlamp was elevated to about 45°, but the temperature stayed at about 25° when aqueous solutions were irradiated with the sunlamp or on exposure to sunlight. In another study, the temperature of the chromatoplate during irradiation was maintained at about 10° by supporting the glass on a cold surface.

Two combinations of tlc solvent systems (X and Y) were used in two-dimensional development for identification of the photoproducts by cochromatography and for their quantitative determination by lsc. The photoproducts were recovered from filter paper by extraction with acetone and from the glass surface by dissolving them in dioxane. The photoproducts in aqueous solution were recovered for tlc analysis by addition of sodium chloride and extraction with dichloromethane.

In studies on possible retardants for resmethrin photodecomposition, the origin of a tlc plate was spotted, in sequence, with hexane or acetone solutions containing 1 μg of antioxidant or uv screening agent, 1 μg of *trans*-[^{14}C]resmethrin and 1 μg of the same or different antioxidant or uv screening agent. The plates were irradiated with a sunlamp for 90 min and then developed with solvent system M for analysis. In another experiment the spotted chromatoplate was irradiated for 90 min either directly with a sunlamp or through a soft glass plate or a Pyrex glass plate.

Bioassays. Adult female houseflies (*Musca domestica* L., 3–4 days after emergence, SCR susceptible strain) were treated topically on the thorax with 1 μl of acetone containing the test compound. Male albino Swiss-Webster mice (20–22 g) were administered the test compound intraperitoneally (ip) using 20–50 μl of methoxytriglycol as the vehicle. Mortality observations were made after 48 hr.

RESULTS

Isolation and Identification of Photoproducts of Unlabeled Resmethrin. (+)-*cis-Resmethrin.* Examination of the photoproducts of (+)-*cis*-resmethrin exposed to sunlight on silica gel plates led to identification of the following compounds: a large amount of *cis*-CA but not any *trans*-CA; small amounts of benzaldehyde and phenylacetic acid; two oxidized esters. *cis*-CA was identified by its ir and nmr spectra and by tlc. Benzaldehyde was converted to its 2,4-dinitrophenylhydrazone [identical ir and mp (142–143°) with those of an authentic sample; mixture melting point with authentic sample not depressed]. Phenylacetic acid was tentatively identified by tlc (solvent system G) and its characteristic odor. One of the ester products was found to be compound I-c (Figure 2) based on its identity with a product, described earlier, from sensitized photooxidation of (+)-*cis*-resmethrin in the following respects: nmr and ir and tlc in solvent systems E, G, and H. However, the product isolated from the sunlight exposure on silica gel did not crystallize. The other oxidized ester was identified as 5-benzyl-5-hydroxy-2-oxo-2,5-dihydro-3-furylmethyl *cis*-chrysanthemate (compound V-c). The nmr spectrum was similar to that of compound III-c except for an extra methyl signal due to the methoxy group in III-c. Compound V-c had the following characteristics: nmr ($CDCl_3$) δ 1.21 (6 H, s), 1.65 (1 H), 1.71 (6 H, d, J = 2 Hz), 1.94 (1 H), 3.19 (2 H, s), 4.69 (2 H, d, J = 2 Hz), 5.30 (1 H, d, J = 7.5 Hz), 6.91 (1 H, m), and 7.25 ppm (5 H, s); ir (direct) 3370 (OH) and 1725–1763 cm^{-1} (ester C=O and α,β-unsaturated γ-lactone).

(+)-*trans-Resmethrin.* The major portion (1.4 g) of the photodecomposed (+)-*trans*-resmethrin eluted from the silicic acid column with 5% ether in hexane. Examination

of this material by tlc revealed resmethrin and CA as major components and some minor compounds including benzaldehyde. The product with the same R_f value as benzaldehyde with solvent systems D and E using uv detection gave an orange spot when sprayed with 2,4-dinitrophenylhydrazine–sulfuric acid solution. The presence of benzaldehyde was confirmed by glc examination of this fraction without further purification in comparison with an authentic sample of benzaldehyde (T_r 2.7 min on 3% SE-30 at 70° and 6.0 min on 10% DC-200 at 80°). The total amount of benzaldehyde was estimated by glc to be about 30 mg. Phenylacetaldehyde which might be a possible precursor of phenylacetic acid was not detected.

This early-eluting material from the silicic acid column was dissolved in ether and washed with 5% sodium carbonate solution to separate neutral and acidic fractions. *trans*-Resmethrin (200 mg) was isolated from the neutral fraction by preparative tlc with solvent system D and characterized by nmr and ir while *cis*-resmethrin was not detected. A minor ester component of the neutral fraction is discussed below. The acidic fraction (423 mg) was almost pure *trans*-CA and contained no *cis*-CA (nmr and tlc with solvent systems D, E, and K).

An oxidized ester (49 mg) in the neutral fraction chromatographing on preparative tlc just below resmethrin was identified as 2-benzyloxy-5-oxo-2,5-dihydro-3-furylmethyl *trans*-chrysanthemate (compound VI-t) based on the following evidence. The ir spectrum indicated an α,β-unsaturated γ-lactone group (strong absorptions at 1760 and 1788 cm^{-1}) and an ester group but no hydroxyl group. The mass spectrum (70 eV) indicated a mol wt of 370 and major fragments including the following: 355 ($M - CH_3$) and 327 ($M - C_3H_7$) as expected on fragmentation of the side chain of CA; 279 ($M - C_7H_7$) and 264 ($M - C_7H_7 - CH_3$); 167, 151, and 123 from the acid moiety. The nmr data established the presence of the *trans*-CA moiety and phenyl group and provided the necessary information for the structural assignment when run without and with addition of two increasing amounts of shift reagent, the results of which are given in sequence: nmr (CCl_4) δ 1.15 (3 H, s), 1.24 (3 H, s), 1.33 (1 H, d, J = 6 Hz), 1.71 (6 H, s), 2.00 (1 H, d of d, J = 6, 7.5 Hz), 4.77 (2 H, q, J = 12 Hz), 4.81 (2 H, s), 4.8 (1 H), 5.78 (1 H, s), 5.98 (1 H, s), and 7.29 ppm (5 H, s). The two independent singlets at δ 5.78 and 5.98 were assigned to the α proton of the α,β-unsaturated γ-lactone and the proton on the carbon bearing two oxygens. Addition of the shift reagent resolved the signal of the cyclopropane proton on the carbon bearing the carboxyl group at δ 1.33 in the original spectrum to show a clear doublet at δ 1.46 (1 H, d, J = 6 Hz). By addition of further shift reagent, the signals near δ 5 were completely separated into individual signals to clearly show their respective coupling patterns: δ 4.95 (1 H, d, J = 8 Hz, olefinic proton of *trans*-CA moiety), 5.53 (2 H, q, J = 12 Hz), and 6.00 ppm (2 H, s). The quartet at δ 5.53, assigned to the protons of the methylene group between the ester group and the double bond, showed the large geminal coupling constant of J = 12 Hz due to the anisotropic effect from adjacent portions of the molecule. The two-proton singlet at δ 6.00 was assigned to the methylene of the benzyloxy group.

A mixture of resmethrin photoproducts (250 mg) eluting from the silicic acid column with 15% ether in hexane was separated on preparative tlc with solvent systems E and H into two oxidized esters, an alcoholic component and a mixture of acids. The first ester, a light yellow viscous oil (60 mg), is the trans isomer of compound I based on comparison of the spectral data with those of the cis isomer I-c previously noted: mass spectra (70 eV) m/e (rel intensity) 354 (64), 339 (2), 336 (4), 123 (100), 122 (36), 107 (31), 91 (50), 81 (48), 77 (21); nmr (CCl_4) δ 1.16 (3 H, s), 1.25 (3 H, s), 1.41 (1 H, d, J = 5.5 Hz), 1.70 (6 H, s), 2.04 (1 H, d of d, J = 5.5, 6 Hz, decoupled to a doublet by irradiation at δ 4.86), 3.34 (1 H, d, J = 3 Hz, decoupled to a singlet by irradiation at δ 4.62), 4.62 (1 H, br), 4.86 (1 H, d), 4.92 (2 H, s), 6.01 (1 H, s), and 6.85–7.35 ppm (5 H, m); ir (direct) 3400 (OH), 1690–1720 (α,β-unsaturated and ester C=O), and 1625 cm^{-1} (C=C). The second ester, slightly more polar than compound I-t, was repurified on 0.5-mm thick tlc plates with solvent system H to give 50 mg of viscous oil. This compound was identified as V-t: mass spectra (70 eV) m/e (rel intensity) 370 (10), 352 (6), 204 (38), 186 (33), 185 (54), 167 (34), 151 (75), 123 (100), 122 (37), 107 (36), 91 (81); nmr ($CDCl_3$) δ 1.13 (3 H, s), 1.21 (3 H, s), 1.35 (1 H, d, J = 5.5 Hz), 1.70 (6 H, s), 2.01 (1 H, d of d, J = 5.5, 6 Hz, decoupled to a doublet by irradiation at δ 4.85), 3.17 (2 H, s), 4.62 (2 H, s), 4.85 (1 H, d), 6.83 (1 H, m), and 7.18 ppm (5 H, s); ir (direct) 3350 (OH) and 1720–1770 cm^{-1} (ester C=O and α,β-unsaturated γ-lactone).

The alcoholic component (16 mg), isolated from the tlc zone between compounds I-t and V-t, was identified as benzyl alcohol (identical nmr and ir with those of an authentic compound). The tlc zone below compound V-t contained only acidic compounds (20 mg) which gave an nmr spectrum appropriate for a mixture of benzoic and phenylacetic acids along with small amounts of impurities. Each component was isolated by preparative tlc using solvent system K and examined as the free acid or after reaction with diazomethane. The acid from the upper band was benzoic acid identified as the methyl ester by glc in comparison with an authentic sample of methyl benzoate (T_r 5 min on 3% SE-30 at 90°). The acid from the lower band was phenylacetic acid identified by nmr and ir and also by conversion to methyl phenylacetate and then glc comparison with an authentic sample of this compound (T_r 3.75 min on 3% SE-30 at 110°).

Most of the other column fractions, especially the more polar ones, consisted of compounds poorly resolved on tlc or in insufficient amount for further examination. All of the fractions from the silicic acid column were specifically examined for the possible presence of BFA, BFCA, α-OH-BFCA, and α-keto-BFCA using two-dimensional tlc with combinations of solvent systems E, H, I, J, and K; however, not any one of these compounds was found. As BFCA and phenylacetic acid behave quite similarly on tlc, samples isolated from the zone close to that of phenylacetic acid were extensively examined by nmr, but BFCA was not detected.

Colorimetric Detection of Epoxides. Epoxyresmethrin was not found in the studies described above but it may be unstable under the column chromatographic conditions utilized. Accordingly, the epoxy esters were sought in experiments involving the spotting of various amounts (20–400 μg) of (+)-*trans*-resmethrin on silica gel 60 chromatoplates and irradiation with a sunlamp for 2 hr followed by two tlc developments with solvent system A and use of the epoxide spray reagent. Both the R and S isomers of epoxyresmethrin were detected at all levels of resmethrin irradiated but not with nonirradiated resmethrin. The R_f values of the epoxyresmethrin isomers formed on photodecomposition were completely identical with those of the authentic R and S isomers not only in solvent system A but also in solvent systems E and F.

(+)-*trans*-Ethanoresmethrin and (+)-*trans*-S-2539 were also converted under these conditions to their epoxy esters, both the R and S isomers being detected in each case with two tlc developments with solvent system A.

Photodecomposition of [^{14}C]Resmethrin. *Photoproducts of trans-Resmethrin.* Exposure of residual deposits of radioactive (+)- or (−)-*trans*-resmethrin to sunlamp irradiation on silica gel 60 chromatoplates for 90 min produced 11 photoproducts identified by tlc cochromatography using development procedures X and Y (for R_f values in the various components of these systems, see Table I). Seven of these are esters detected equally with the acid-

Table I. Chromatographic Characteristics of *trans*-Resmethrin, Its Photoalteration Products, and Related Compounds on Silica Gel 60 F-254 Thin-Layer Chromatoplates

Compound	R_f values in indicated solvent systems[a]			
	C + K	F + F	F	A + A
Esters				
trans-Resmethrin	0.74	0.81	0.79	0.67
trans-Epoxyresmethrin (*R* isomer)	0.66	0.75	0.68	0.24
trans-Epoxyresmethrin (*S* isomer)	0.69	0.78	0.71	0.32
Cyclopentenolone (I-t)	0.45	0.50	0.36	0.02
Hydroxy lactone (V-t)	0.50	0.24	0.12	0.01
Benzyloxy lactone (VI-t)	0.68	0.78	0.71	0.14
Epoxide of cyclopentenolone (VII-t) (*R* isomer)	0.24	0.30		
Epoxide of cyclopentenolone (VII-t) (*S* isomer)	0.28	0.29		
Unknown ester α	0.43	0.55	0.42	0.02
Cleavage Products				
trans-CA	0.58	0.25	0.12	0.08
cis-CA[b]	0.62	0.31		
BFA[b]	0.42	0.46	0.39	0.04
BFCA[b]	0.37	0.05		
Phenylacetic acid	0.37	0.05		
Benzyl alcohol	0.44	0.42	0.38	0.07
Benzoic acid	0.48	0.06		

[a] The tlc solvent systems (see text) are designated in the order of use when two sequential developments were made. [b] Not formed on *trans*-resmethrin photodecomposition.

and alcohol-labeled preparations: the *R* and *S* isomers of *trans*-epoxyresmethrin; compounds I-t, V-t, and VI-t, which are each oxidized *trans*-chrysanthemates; the *R* and *S* isomers of the epoxide of the cyclopentenolone, compound VII-t. One of them, detected only with acid-labeled resmethrin, is *trans*-CA. Three products, detected only with the alcohol-labeled preparation, are benzyl alcohol, benzoic acid, and phenylacetic acid. Chrysanthemum dicarboxylic acid and benzaldehyde were not detected as photoproducts; the inability to detect benzaldehyde may be due to its volatility and ease of oxidation when present in small amounts.

Rate Studies with trans- and cis-Resmethrin. The trans and cis isomers of resmethrin decompose at similar rates when irradiated on silica gel, giving *trans*- and *cis*-CA, respectively (Figure 3). The tlc patterns of other photoproducts are quite similar for *trans*- and *cis*-resmethrin developing twice in the same direction, first with solvent system C and then with K.

trans-Resmethrin undergoes very little decomposition on silica gel chromatoplates in the dark; after 150 and 430 min the percentage recoveries are 98 and 97%, respectively, for the total radiocarbon of which 97 and 95%, respectively, is accounted for as resmethrin. However, on exposure to sunlamp irradiation, resmethrin on silica gel undergoes extensive photodecomposition; after 420 min of irradiation when 88% of the applied radiocarbon is recovered, only 5% of the recovered radioactivity is resmethrin, 48% is ester photoproducts, 14% is nonester photoproducts, and 32% is not characterized (Figure 4). The identified photoproducts present after 420 min of irradiation account for 43% of the total recovery of which 33% are esters and 10% are nonester products. Many of the unidentified photoproducts are esters based on their chromatographic behavior and their detection in similar amounts with both acid- and alcohol-labeled compounds.

The photoproduct found in largest amount is the cyclopentenolone ester (compound I-t), accounting for about one-fifth of the applied material after irradiation for 250

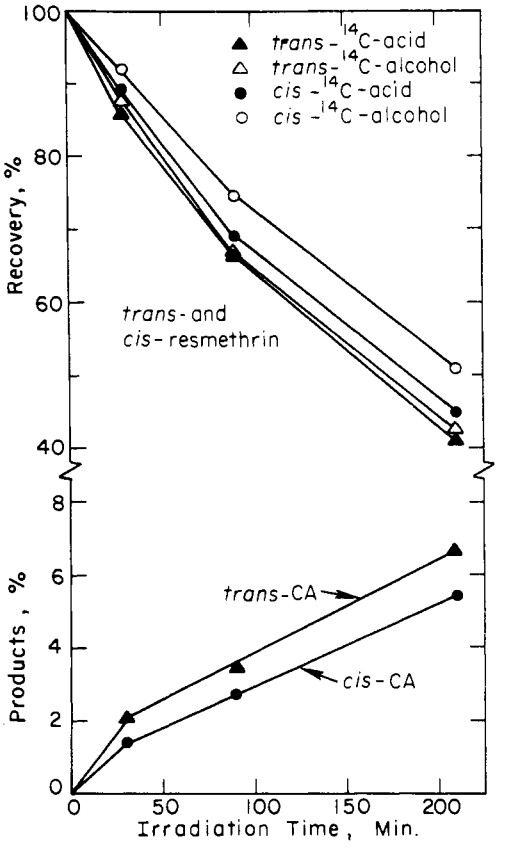

Figure 3. Rates of photodecomposition of *trans*- and *cis*-resmethrin and formation of *trans*- and *cis*-chrysanthemic acids on silica gel chromatoplates irradiated with a sunlamp.

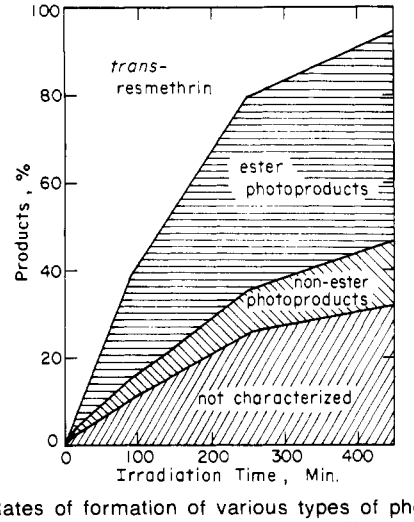

Figure 4. Rates of formation of various types of photoproducts on *trans*-resmethrin photodecomposition on silica gel chromatoplates irradiated with a sunlamp.

and 420 min (Figure 5A). The unidentified ester photoproduct α and *trans*-CA are formed in relatively large amounts (Figure 5A). Four other oxidized esters with modified alcohol moieties accumulate slowly but not to high levels (Figure 5B). The epoxyresmethrin isomers are minor and do not accumulate; although these compounds are detected even on holding in the dark at 22° (Figure 5C), the amount produced by irradiation for 120 min under cooling (10°) exceeds that of the control by two- to fourfold. The lag phase prior to formation of increasing amounts of the isomeric epoxides of the cyclopentenolone ester, compound VII-t (Figure 5B), is as expected since they are formed from the epoxyresmethrin isomers and

Table II. Recovery of Individual Products following Irradiation of *trans*-Resmethrin on Silica Gel, Glass Plates, or Filter Paper or as a Solution in Water with a Sunlamp or Sunlight

Compound	Amt of individual product rel to total recovd radiocarbon, %[a]				
	Sunlamp				Sunlight
	90, silica gel	90, glass plate	90, filter paper	60, water	15, silica gel
trans-Resmethrin	62 (98)[b]	68 (96)	36 (92)	75 (90)	71 (99)
trans-Epoxyresmethrin (*R* isomer)	1.3 (0.4)	1.3 (1.1)	6.2 (1.3)	5.2 (2.8)	0.5 (0.3)
trans-Epoxyresmethrin (*S* isomer)	1.7 (0.2)	1.3 (0.2)	0.7 (0.1)	0.4 (0.2)	0.4 (0.1)
Cyclopentenolone (I-t)	13 (0.3)	1.0 (<0.1)	1.7 (0.5)	<0.1	3.8 (0.2)
Hydroxy lactone (V-t)	1.2 (0.1)	3.2 (<0.1)	2.0 (<0.1)	<0.1	4.2 (0.1)
Benzyloxy lactone (VI-t)	0.9 (<0.1)	1.5 (0.1)	1.5 (0.1)	<0.1	0.4 (<0.1)
trans-CA	3.3 (0.4)	3.6 (0.3)	5.8 (<0.1)	11 (3.4)	4.3 (0.2)

[a] Average of values obtained with acid- and alcohol-labeled (+)- or (−)-*trans*-resmethrin except in the case of *trans*-CA where the results are based on the acid-labeled preparation, only. The remainder of the recovered radiocarbon was present as photoproducts other than those tabulated. The total recoveries of applied radiocarbon were 91–93% on silica gel or glass plates, 72% on filter paper, and 81% in water. Conditions given are light source, irradiation time (minutes), and medium. [b] The values in parentheses are the results obtained under identical conditions in the absence of light.

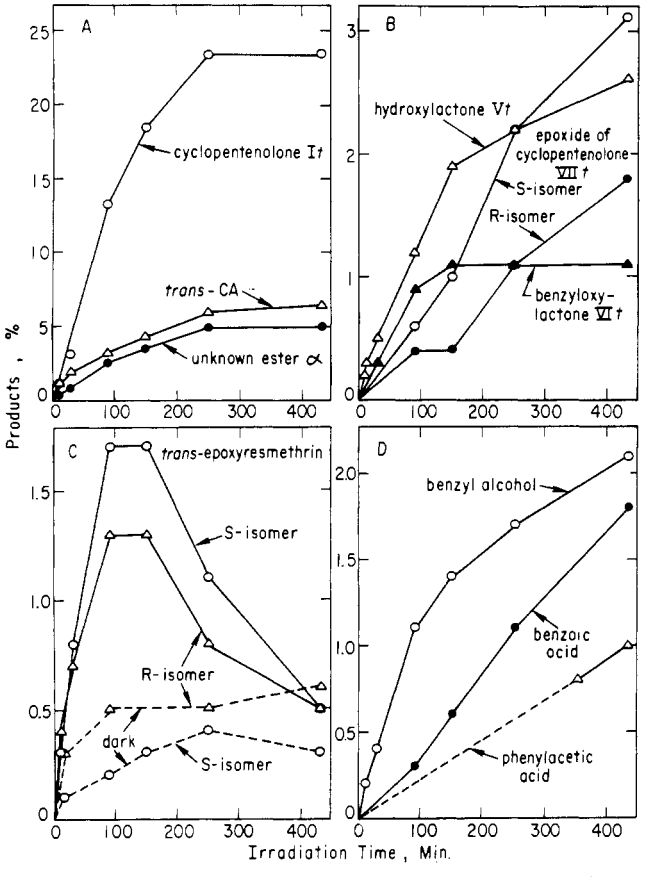

Figure 5. Amounts of individual photoproducts formed on *trans*-resmethrin photodecomposition on silica gel chromatoplates irradiated with a sunlamp. The percentage values are relative to the recovered radiocarbon with acid- or alcohol-labeled resmethrin, as appropriate: (A) major photoproducts; (B) esters with oxidized alcohol moieties; (C) epoxyresmethrin isomers comparing amounts in the dark and on sunlamp irradiation; (D) phenyl-containing fragments from alcohol moiety.

from compound I-t (Figures 5A and 5C). Photoproducts resulting from extensive decomposition of the alcohol moiety, such as phenylacetic acid, benzoic acid, and benzyl alcohol, tend to increase in amount even after resmethrin has almost completely disappeared (Figure 5D); it is assumed in this study that the product assigned as phenylacetic acid contains no BFCA, which would chromatograph in the same position, since no BFCA was found by other techniques as reported above.

The photoproduct distribution pattern is similar using sunlight or sunlamp irradiation except for an increased level of compound V-t present on sunlight irradiation. The pattern of products, however, is greatly dependent on the supporting material or medium. The cyclopentenolone (compound I-t) is present in large amounts only on silica gel plates while the epoxides appear in relatively large amounts only when the exposure is on filter paper or in water in which case the level of *R* isomer exceeds that of the *S* isomer by 9- to 13-fold (Table II).

Table III. Recovery of Original Esters and *trans*-Chrysanthemic Acid following Irradiation of Acid-Labeled *trans*-Resmethrin, *trans*-Tetramethrin, and *S*-Bioallethrin on Silica Gel Chromatoplates with a Sunlamp or Sunlight

Irradiation conditions	Recovery of original ester, %		
	Resmethrin	Tetramethrin	Allethrin
Sunlamp			
30 min, <45°	75	84	93
90 min, <45°[a]	37 (11)[b]	37 (0.3)[b]	82 (0.9)[b]
90 min, 10°	28	88	91
Sunlight			
15 min, 25°[a]	26	87	89

[a] The results are the average of three experiments for the 90-min sunlamp irradiation and two experiments for the 15-min sunlight irradiation. All other values are from single experiments. [b] Percentage recovery of *trans*-CA.

Attempts to Inhibit the Photodecomposition of trans-Resmethrin. The photodecomposition of *trans*-resmethrin on silica gel plates was not altered nor was the product ratio greatly changed by uv screening agents [2-hydroxy-4-(2-hydroxy-3-methacrylyloxy)propoxybenzophenone, ethyl cinnamate, and benzyl cinnamate] and antioxidants [2,6-dioctadecyl-*p*-cresol and 2,6-di-*tert*-butyl-*p*-cresol]. Filtration of the light irradiating chromatoplates spotted with resmethrin slightly increased the recovery of undecomposed resmethrin, from 61% for unfiltered light to about 80% for light filtered through a soft glass or Pyrex glass plate. Light filtration through soft or Pyrex glass also reduced the formation of the major photoproduct (compound I-t) from 13 to 5%.

Relative Rates of Photodecomposition of Various Pyrethroids. The photodecomposition rates were compared for 14-μg/cm^2 residual deposits of *trans*-resmethrin, *trans*-tetramethrin, and *S*-bioallethrin (Table III). The acid-labeled esters were spotted as ethanol solutions to minimize distribution differences on the silica gel 60 chromatoplates. The total radiocarbon recoveries for these compounds varied from 99 to 102%. *S*-Bioallethrin is the most stable of these compounds under all test conditions. *trans*-Tetramethrin is more persistent than *trans*-resmeth-

Table IV. Toxicity of Three Pyrethroids and Their Epoxy Derivatives to Houseflies Treated Topically

Pyrethroid	LD_{50}, μg/g: Chrysanthemate	Epoxychrysanthemate: *R* isomer	Epoxychrysanthemate: *S* isomer
(+)-*trans*-Ester			
Resmethrin	0.8	>16	>16
Ethanoresmethrin	0.4	5	20
S-2539	2.6	>180	>180
(+)-*cis*-Ester			
Resmethrin	1.8	>115	>115
Ethanoresmethrin	0.6	40[a]	
S-2539	3.8	45,160[b]	

[a] *R* and *S* isomer mixture in equal amounts based on nmr analysis. [b] The values are given on the separated *R* and *S* isomers but their configuration is not individually assigned. The more toxic isomer is the one of lower tlc R_f value in solvent system D.

Table V. Composition and Intraperitoneal Toxicity to Mice of Photodecomposed (+)-*trans*-Resmethrin

Irradiation time, hr[a]	Composition, %: Resmethrin	Composition, %: (+)-*trans*-CA	LD_{50}, mg/kg
	Photodecomposed Resmethrin		
2	78	5	1800
3	39	18	1200
5	43	12	960
15	0	6	580
	Comparison Compounds		
0	100	0	>2500
0	0	100	98

[a] The exposure times of 2 and 5 hr were on a hazy day while those of 3 and 15 hr were on clear days.

rin except when the exposure temperature is elevated on exposure to the sunlamp. For some unexplained reason, tetramethrin is more temperature sensitive than the other pyrethroids in the presence of light. Only resmethrin gave an appreciable amount of CA, in fact an amount threefold higher than in the studies discussed above at comparable irradiation times. The use of ethanol solutions in spotting may have resulted in a more uniform distribution of resmethrin exposed to the light than in the other studies. *trans*-Tetramethrin gave only two major photoproducts, the *R* and *S* isomers of *trans*-epoxytetramethrin; these epoxytetramethrin isomers accounted for 40% of the applied radioactivity and 88% of the photoproducts after 90-min irradiation with a sunlamp without temperature control.

It was surprising to find that *trans*-tetramethrin is highly susceptible to photoepoxidation but *S*-bioallethrin is not, even though both compounds have the same acid moiety. It was considered possible that *trans*-tetramethrin or certain of its photoproducts act catalytically to enhance photoepoxidation or, alternatively, *S*-bioallethrin or photoproducts of this compound inhibit photoepoxidation. However, neither of these possibilities appears to be the case since the patterns of photolysis products of *trans*-[^{14}C]tetramethrin and *S*-[^{14}C]bioallethrin were not altered on fortification with up to six times the amount of unlabeled *S*-bioallethrin and *trans*-tetramethrin, respectively. An alternative possibility is that an intramolecular interaction occurs involving the conjugated carbonyl system of tetramethrin and the isobutenyl double bond.

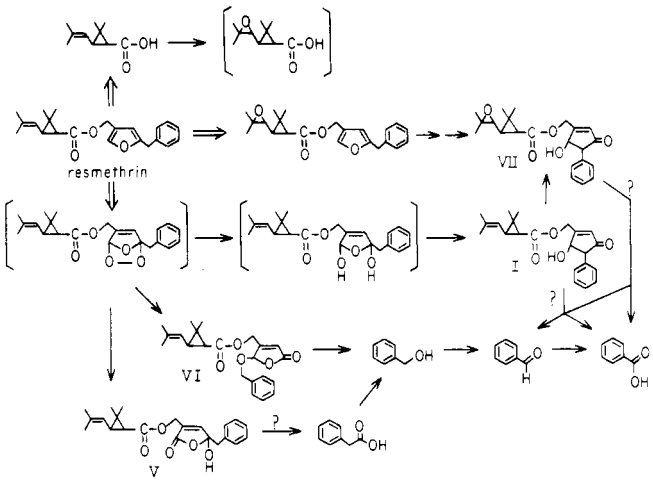

Figure 6. Photodecomposition pathways of resmethrin. The chemical names of compounds designated by Roman numerals are given in the text where the letters t and c are used after the Roman numerals to show that the compounds are derived from *trans*- and *cis*-resmethrin, respectively.

Toxicity of Photoproducts. The housefly toxicity of the photoproducts is very low relative to the parent pyrethroid. (+)-*trans*-Resmethrin gives a LD_{50} value of 0.8 μg/g while each of the following photoproducts of (+)-*trans*-resmethrin gives no mortality at 40 μg/g: photoproducts I-t, V-t, and VI-t; the mixture of photoproducts containing no resmethrin after 23-hr exposure on a silica gel 60 chromatoplate at 0.5 mg/cm^2. The epoxy derivatives are also greatly reduced in toxicity to houseflies (Table IV); this confirms the findings of Elliott *et al.* (1972). The *R* isomer is more toxic than the *S* isomer of (+)-*trans*-epoxyethanoresmethrin and the epoxy isomers of (+)-*cis*-S-2539 also differ in toxicity.

One of the (+)-*trans*-resmethrin photoproducts, (+)-*trans*-CA, is more toxic to mice treated intraperitoneally (ip) than the parent compound. The ip LD_{50} values of (+)- and (−)-*trans*- and (+)-and (−)-*cis*-CA are 98, 435, 600, and 410 mg/kg, respectively. The mixtures of photodecomposition products after various irradiation times are also more toxic than the parent (+)-*trans*-resmethrin though they are still relatively low in toxicity (Table V). The toxicity of the photoproducts is not attributable only to (+)-*trans*-CA since the LD_{50} values do not coincide with the content of this acid (Table V); other toxicants must also be present among the photoproducts.

DISCUSSION

The photodecomposition pathways of resmethrin deduced from the identified photoproducts are shown in Figure 6. The initial pathways are of three types: (1) oxidation of the furan ring to give a cyclic ozonide-type peroxide intermediate, (2) epoxidation of the isobutenyl double bond, and (3) cleavage at the ester linkage to give CA.

The cyclic ozonide-type peroxide, an intermediate in photosensitized oxidation of other furan derivatives (Foote *et al.*, 1967), is probably involved in photooxidation of resmethrin based on the identified oxidized esters which can originate from this compound. Migration of the benzyl cation or radical gives the benzyloxy lactone (VI). Migration of a proton or a hydrogen radical from the position symmetrical to the benzyl group gives the hydroxy lactone (V). Reduction of the cyclic peroxide to the diol intermediate, followed by rearrangement, gives the cyclopentenolone (I). The phenyl-containing fragments from the alcohol moiety such as phenylacetic acid, benzyl alcohol, benzaldehyde, and benzoic acid are formed by extensive oxidation of the esters but pathways other than those shown in Figure 6 might also exist. The sequence of photodecompo-

sition in water from phenylacetic acid to benzoic acid *via* benzyl alcohol and benzaldehyde is known from a previous study (Crosby and Leitis, 1969). The photoreactions of the alcohol moiety are likely to be applicable not only to resmethrin but also to ethanoresmethrin and other 5-benzyl-3-furylmethyl esters. The unpleasant odor of photodecomposed resmethrin and ethanoresmethrin, either cis or trans isomers or technical material, and of other photodecomposed 5-benzyl-3-furyl compounds appears to be due, at least in part, to the photochemical formation of phenylacetic acid.

While a variety of photooxidations of the chrysanthemate moiety are known (Chen and Casida, 1969), it appears that the isobutenyl double bond or comparable group in related acid moieties is the most labile to photodegradation in an oxygen atmosphere; the high degree of epoxidation of tetramethrin is most remarkable in this respect. Cleavage of the ester linkage, a photochemical process since it does not occur in the dark, may be a characteristic of resmethrin and related BFA esters; ester cleavage was negligible with allethrin and tetramethrin. Cleavage by a simple photohydrolysis reaction would yield BFA, but none is found; this indicates either that a more complex cleavage mechanism is involved or that BFA is not sufficiently stable to accumulate.

It is well known that solutions of CA and certain of its simple esters and amides undergo photochemical isomerization when irradiated with uv light with or without photosensitizers in the absence of oxygen (Bullivant and Pattenden, 1971; Sasaki *et al.*, 1968; Ueda and Matsui, 1971). In the present study, involving irradiation on silica gel plates with sunlight or a sunlamp in the presence of oxygen, not any evidence of isomerization was found with resmethrin in accord with an earlier study on other pyrethroid insecticides (Chen and Casida, 1969).

Resmethrin is more stable than allethrin and tetramethrin when irradiated as a 13-mg/cm^2 film on a glass dish with a lamp which simulates sunlight (Abe *et al.*, 1972). In the present study, however, resmethrin is quite unstable compared to allethrin and tetramethrin. The differences in these two studies may be due in part to the available surface area relative to weight of pyrethroid and the nature of the supporting material each of which will determine the oxygen availability. There are large differences in the rate of resmethrin photodecomposition and in the ratios of the photoproducts under different conditions. It is obvious, therefore, that the results of the present study cannot be extrapolated directly to the variety of environmental conditions potentially involved in the use of this insecticide chemical. However, they are useful in interpreting the results of environmental persistence studies.

The toxicity of natural pyrethrins, allethrin, and tetramethrin to houseflies (topical) and mice (ip) is decreased on photodegradation (Chen and Casida, 1969). Photodegradation also greatly reduces the toxicity of resmethrin to houseflies but it increases the ip toxicity to mice. When assayed by oral administration, however, the toxicity of the mixture of photoproducts of (±)-*trans,cis*-resmethrin to mice is less than that of the original compound (Brown, 1973). Thus, the mammalian toxicity of photodecomposed resmethrin appears to depend on the route of administration.

There has been some success in prolonging the persistence of allethrin and the natural pyrethrins by formulating with protective adjuvants or stabilizers (Abe *et al.*, 1972; Miskus and Andrews, 1972). Addition of uv screening agents and antioxidants did not stabilize resmethrin to photodecomposition possibly due to the fact that the mechanism of photodegradation of resmethrin is different from that of natural pyrethrins and allethrin. With resmethrin, the furan portion of the molecule contributes the major part of the photolability due to both its oxidation and ability to facilitate ester cleavage. Pyrethroids lacking these photolabile groupings might have improved utility in some areas of insect control.

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