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Photochemistry of Ethofenprox and Three Related Pyrethroids with Ether, Alkane, and Alkene Central Linkages

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The pyrethroid insecticide ethofenprox (MTI-500) [2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether] undergoes two primary photochemical processes at the central $-C(CH_3)_2CH_2OCH_2-$ ether linkage, depending on the irradiation conditions. In oxygenated solutions or thin films the major process is benzylic oxidation to give the corresponding central $-C(CH_3)_2CH_2OC(O)-$ ester linkage. In deaerated solutions the loss of CH_2O predominates to form the central $-C(CH_3)_2CH_2-$ alkane linkage. These appear to be detoxification reactions. Seven other characterized photoproducts of ethofenprox are formed on cleavage of the central linkage without alteration of the ethoxy or phenoxy moiety. MTI-800 [1-(3-phenoxy-4-fluorophenyl)-4-(4-ethoxyphenyl)-4-methylpentane] with the central $-C(CH_3)_2(CH_2)_3-$ alkane linkage is generally more photostable than ethofenprox. Two tentatively identified photoproducts of MTI-800 are formed by elimination of the phenoxy group, giving the fluorophenyl analogue, and photocyclization, yielding the corresponding dibenzofuran. Structurally analogous alkenes with the $-(\overline{CCH_2CH_2})-CH=CHCH_2-$ central linkage are more photolabile than ethofenprox, undergoing isomerization and oxidation at both the *E* double bond and the cyclopropyl group.

Conventional pyrethroids have central ester groups, but high insecticidal activity is also observed in compounds with alternative central linkages such as suitable ether, alkane, and alkene substituents. Examples of these non-ester pyrethroids are the ether ethofenprox (1) (also known as MTI-500 and Trebon) (Nakatani et al., 1982; Udagawa, 1986), the alkane MTI-800 (2) (Udagawa et al., 1985), and the alkenes NRDC 199 (3) and 200 (4) (Elliott, 1985). Compounds 1 and 2 have two useful properties relative to the ester pyrethroids, i.e., reduced toxicity to mammals and aquatic species and enhanced photochemical stability (Udagawa et al., 1985; Yano et al., 1986).

1: 2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether
2: 1-(3-phenoxy-4-fluorophenyl)-4-(4-ethoxyphenyl)-4-methylpentane
3 (R = Cl) and **4** (R = OEt): 1-(4-chloro- or -ethoxyphenyl)-1-[(*E*)-(3-phenoxy-4-fluorophenyl)prop-1-enyl]cyclopropane

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This report examines the photodecomposition rates and products obtained on irradiation of 1–4 in various solvents and as thin films in the solid phase, focusing on the processes of ethofenprox, currently the most important of the nonester pyrethroids.

MATERIALS AND METHODS

Chromatography. Thin-layer chromatography (TLC) for monitoring reactions and isolation of photoproducts employed silica gel 60 F-254 precoated chromatoplates (E. Merck, Darmstadt, Germany; 0.25 or 0.5 mm) developed with hexane–acetone (20:1) or hexane–diethyl ether (20:1). Multiple developments were used for better resolution in preparative separations. Photoproducts were recovered by sonicating the gel in dichloromethane followed by centrifugation.

Liquid adsorption column chromatography (LC) for photoproduct isolation utilized 25 g of silica gel (Merck; 0.063–0.20 mm) and elution with *n*-hexane (100 mL), *n*-hexane–diethyl ether (30:1) (200 mL), and *n*-hexane–diethyl ether (10:1) (100 mL).

Gas–liquid chromatography (GC) for monitoring reaction rates as loss of the parent compound employed a Hewlett-Packard Model 5840A instrument equipped with a packed glass column (3% SP 2100 on Chromosorb, 2 m × 4 mm (i.d.), helium carrier gas 20 mL/min) and a flame ionization detector (FID). High-resolution gas chromatography (HRGC) for product analysis involved a fused silica capillary column (Supelco Inc., Bellefonte, PA; SE 54, 15 m × 0.25 mm (i.d.), 0.25-μm film; helium carrier gas 40 cm/s) with a 2:1 split ratio. Analyses were carried out isothermally with the packed column and by temperature program (90 °C for 3 min, 10 °C/min to 280 °C, and then 280 °C for 10 min) on the SE 54 capillary.

Spectroscopy. HRGC mass spectrometry (HRGC–MS) involved a Hewlett-Packard 5985B system operated under

electron impact (70-eV) conditions. A cross-linked methylsilicone high-performance fused silica capillary (Hewlett-Packard, Avondale, PA; 25 m × 0.2 mm (i.d.), 0.32-μm film; helium carrier gas 30 cm/s) was temperature programmed (90 °C for 3 min, 10 °C/min to 280 °C, and then 280 °C for 10 min) for separation of 1, 2, 4, and their photoproducts; the temperature program was 3 °C/min for 3 and its photoproducts. Photoproduct mixtures were examined directly and after treatment with diazomethane and/or hexamethyldisilazane (HMDS) to form methyl esters and trimethylsilyl (TMS) derivatives, respectively.

Nuclear magnetic resonance (NMR) spectroscopy was carried out on products isolated by TLC and LC using a Bruker WM 300 instrument (300 MHz for ^{1}H and 75 MHz for ^{13}C) with an ASPECT 3000 computer. Samples were dissolved in chloroform-d, and chemical shifts (δ) are reported downfield from tetramethylsilane.

Ultraviolet (UV) spectra for the pyrethroids at 10 mM in methanol were recorded with a Perkin-Elmer 576 ST spectrophotometer. Infrared (IR) spectra were determined as carbon tetrachloride solutions with a Perkin-Elmer 457 IR spectrophotometer.

Chemicals. Sources for the pyrethroids examined were as follows: 1 and 2 from Mitsui Toatsu Chemicals, Inc., Yokohama, Japan; 3 and 4 from N. F. Janes, Rothamsted Experimental Station, Harpenden, Hertfordshire, U.K.; (1R,$trans$)-permethrin from Roussel Uclaf, Paris, France. They were each of >96% purity based on TLC, HRGC-FID, and HRGC-MS either directly as received (1-3, permethrin) or after TLC cleanup (4). No individual impurity in any starting material exceeded 1% in amount. The epoxy derivatives of 3 and 4 were obtained as isomeric mixtures by treating 3 and 4 (10 μmol) with excess m-chloroperbenzoic acid in carbon tetrachloride (1 mL), purification by TLC (hexane–acetone, 10:1, 3×), and characterization by ^{1}H NMR and HRGC-MS. These products gave a blue-violet color when treated with 4-(p-nitrobenzyl)pyridine (Hammock et al., 1974).

Irradiation. Photolyses were carried out at 290–320 nm through Pyrex in a Rayonet reactor equipped with 16 RPR 3000 lamps (The Southern New England Ultraviolet Co., Middletown, CT). Solutions were irradiated at 35 °C in a merry-go-round arrangement to ensure equal exposure. Irradiated samples were compared to "dark" controls (sample tubes wrapped in aluminum foil). The solutions irradiated were 2.5 mM 1 in acetonitrile–water (3:2) and 1 mM 1 in methanol for preparative photolysis and 5–20 mM 1–4 in methanol for rate determinations by GC and product identification by HRGC-MS. Nitrogen or oxygen was bubbled through the methanol solution before and during irradiation. Thin films of 1–4 (1–4 μg/cm^2) were irradiated at 35 °C in Pyrex Petri dishes with covers (9-cm diameter) and in Pyrex flasks (2 L). The photoproducts were then dissolved in dichloromethane and analyzed by GC. Sensitized photolysis of 3 (1 mM) was examined with rose bengal (0.1% w/v) in oxygen-saturated methanol exposed to a 60-W lamp.

Bioassay. Insecticidal activity was assayed with adult female houseflies (*Musca domestica* L.), applying the test compound in 0.5 μL of acetone to the ventrum of the abdomen. To test for synergized toxicity, piperonyl butoxide (PB; 250 μg/g) was topically applied to the same body region 1 h before dosing with the pyrethroid or photoproduct. Mortality determinations were made after 24 h. Goldfish (*Crassius auratus*) (4–5 cm) were used for bioassays under static conditions. The test compound in acetone (0.1–0.5 mL) was injected into 1 L of aerated water containing four fish, and mortality was recorded after 48

Table I. UV Absorbance of 1–4 and (1R,$trans$)-Permethrin in Methanol

compd	ϵ, M^{-1} cm^{-1}		
	290 nm	300 nm	310 nm
1	17	8	3.6
2	21	17	7
3	93	37	22
4	300	47	37
permethrin	160	15	5

Table II. Photoreaction Rates of 1–4 as Methanol Solutions and Extent of Photoreaction as Thin Films at 290–320 nm

compd	methanol/air[a]		thin film,[d] % reactn	
	k,[b] h^{-1}	$t_{1/2}$,[c] h	4 h	20 h
1	0.0049	140	50	85
2	0.0061	110	15	25
3	0.018	40	80	100
4	0.049	14	85	100

[a] Decomposition monitored after 5, 24, 28, 48, 52, and 72 h for 1 at 20 mM, 2 and 4 at 10 mM, and 3 at 5 mM. [b] Rate constant on the assumption of pseudo-first-order decomposition: ln (C/C_0) = ln A - kt. In each case the correlation coefficient was >0.99. [c] Half-life ($t_{1/2}$) = 0.693k^{-1}. (1R,$trans$)-Permethrin (20 mM) under identical conditions shows a $t_{1/2}$ of 50 h. [d] 1 μg/cm^2.
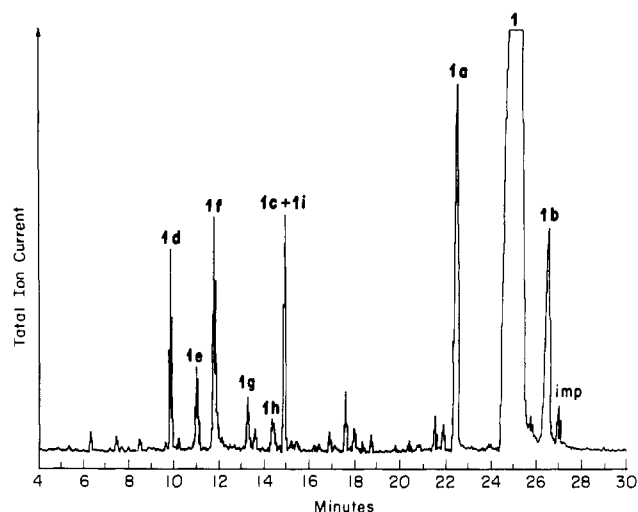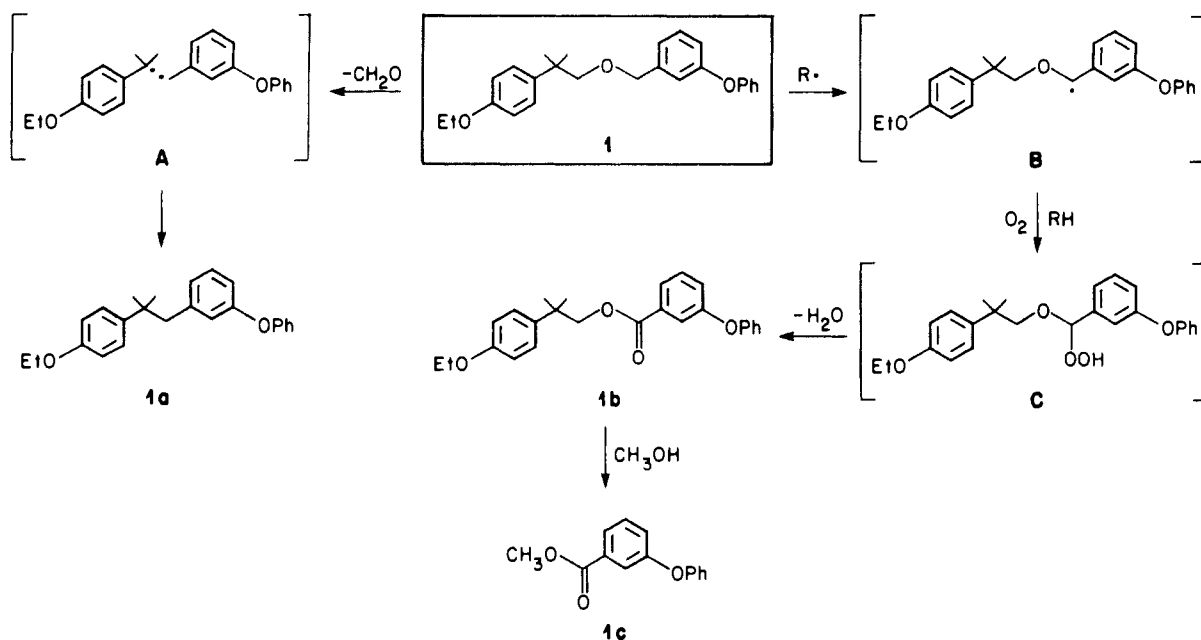

Figure 1. HRGC–MS total ion chromatogram of ethofenprox (1) and its photoproducts. Irradiation in oxygenated methanol for 50 h at 290–320 nm was followed by treatment with diazomethane. The major impurity in solutions of 1 and "dark" control samples is designated as "imp".

h. LD$_{50}$ values for houseflies and LC$_{50}$ values for goldfish were determined from three or more experiments using log dose–probit mortality analysis.

RESULTS

UV Absorbance (Table I). In the environmentally relevant region of 300–310 nm, 1 and 2 with the central ether and alkane linkages show similar absorbance to permethrin, whereas the alkenes 3 and 4 have considerably higher extinction coefficients. At wavelengths greater than 310 nm absorbance decreases continuously for all four compounds.

Photoreaction Rates (Table II). In methanol solutions 1 and 2 are much more photostable than (1R,$trans$)-permethrin, which in turn is somewhat less reactive than 3 and 4. Thin films of 2 are manyfold more stable than those of 1, 3, and 4. Compounds 1 and 2 differ considerably in their photostability as thin films but not as methanol solutions.
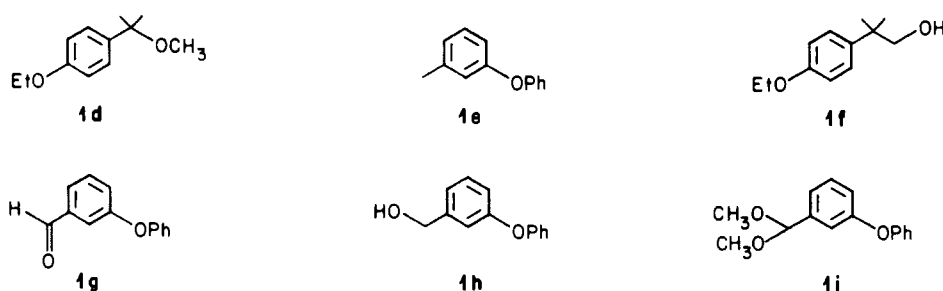
Figure 2. Proposed partial photodegradation pathways and minor photoproducts for ethofenprox (1) with an ether central linkage as solutions in methanol and aqueous acetonitrile and as a thin film. RH is a hydrogen donor.
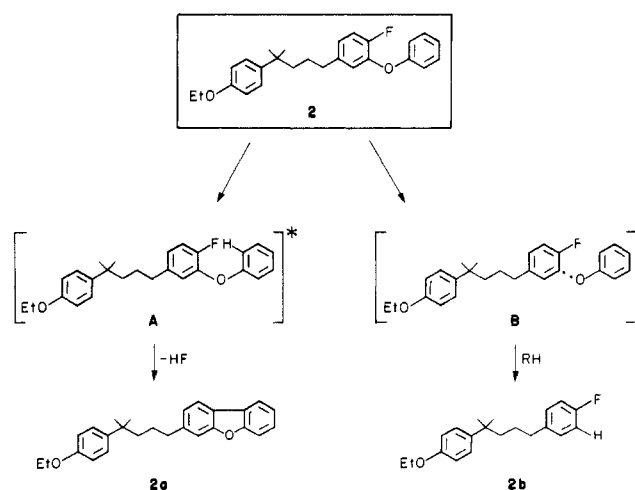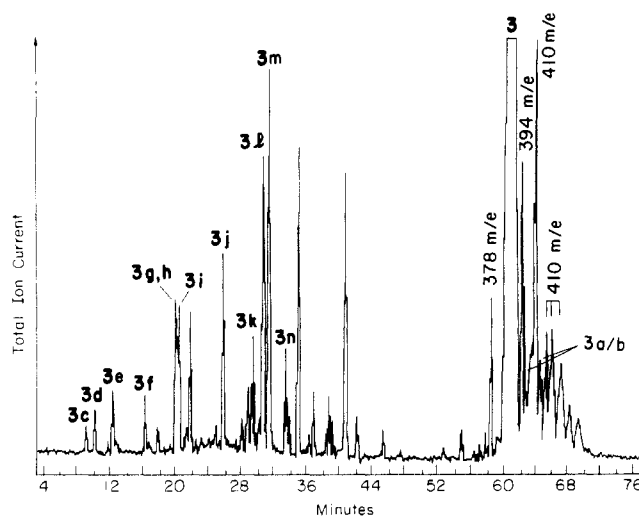

Figure 3. Proposed photodegradation pathways for MTI-800 (2) with an alkane central linkage as a methanol solution and as a thin film. RH is a hydrogen donor.

Chromatography and Identification of Photoproducts. Ether 1 and its photoproducts give an HRGC-MS total ion chromatogram and product identities shown in Figures 1 and 2, respectively. The photoproducts of alkane 2 are illustrated in Figure 3. The chromatogram of alkene 3 and its photoproducts is given in Figure 4, and structures for the photoproducts of alkenes 3 and 4 are shown in Figure 5.

Figure 4. HRGC-MS total ion chromatogram of NRDC 199 (3) and its photoproducts. Irradiation in oxygenated methanol for 50 h at 290–320 nm was followed by treatment with diazomethane. Unidentified photoproducts are indicated with their molecular ions m/e 378, 394, and 410.

The photoproducts were identified by comparison of their mass spectra and HRGC retention times (R_t) with authentic standards and tentatively characterized by interpretation of MS fragmentation patterns. Compounds designated as photoproducts were not present or appeared

Table III. GC and MS Characteristics of Ethofenprox (1) and Its Photoproducts

compd	R_t,[a] min	m/e (relative intensity)	
		M+	important fragments
1	25.2	376 (10)	183 (10), 163 (100), 135 (20), 107 (20)
1a	22.6	346 (5)	183 (5), 163 (100), 135 (20), 107 (20)
1b	26.5	390 (20)	197 (10), 163 (100), 135 (20), 107 (20)
1c	14.9	228 (100)	213 (100), 197 (80), 169 (40), 141 (40), 115 (40)
1d	9.9	194 (10)	179 (100), 163 (20), 151 (30), 135 (20), 121 (15), 107 (20)
1e	11.1	184 (100)	169 (15), 141 (30), 115 (15)
1f	11.8	194 (10)	163 (100), 135 (40), 107 (40)
1g	13.3	198 (100)	197 (40), 181 (30), 169 (40), 141 (40), 115 (30)
1h	14.5	200 (100)	181 (20), 169 (20), 141 (20), 115 (20)
1i	14.9	244 (20)	213 (100), 197 (40), 169 (30), 141 (30), 115 (20)

[a] GC conditions given in Materials and Methods. See Figure 1.

Table IV. GC and MS Characteristics of MTI-800 (2) and Its Major Photoproducts

compd	R_t,[a] min	m/e (relative intensity)	
		M+	other fragments
2	25.5	392 (15)	214 (5), 201 (5), 181 (10), 163 (100), 135 (20), 107 (20)
2a	30.3	372 (30)	181 (30), 163 (100), 135 (20), 107 (20)
2b	18.4	300 (20)	163 (100), 135 (30), 109 (30), 107 (20)

[a] GC conditions given in Materials and Methods.

in trace amounts in the "dark" controls relative to the irradiated samples. Relevant data for the photoproducts of 1–4 are given in Tables III–VI, respectively. MS gave mostly small but detectable molecular ions plus additional information about fragmentation of aid in characterizing the products. Derivatization with diazomethane and HMDS led to identification of the alcohol and carboxylic acid photoproducts as methyl esters and TMS ethers and esters. Table VII gives the characteristic MS fragments of the parent compounds and major photoproducts. NMR spectroscopy served to further confirm the identities of the major photoproducts of 1 (Table VIII).

Photoproducts of 1 (Figures 1 and 2; Tables III, VIII, and IX). The photochemistry of 1 was examined at 290–320 nm for solutions in methanol and acetonitrile–water (3:2) and as thin films. Photolysis in methanol was performed in both the presence and absence of oxygen. Photoproduct yields under the various conditions are given in Table IX as determined by HRGC-FID.

The major photoproduct is 1a [1-(3-phenoxyphenyl)-2-(4-ethoxyphenyl)-2-methylpropane] in deaerated methanol and 1b [2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzoate] in thin films irradiated at 290–320 nm. In a separate study it was found that 1b is also the major

photoproduct on exposure of 1 as a thin film to sunlight for 20 h.

LC on silica gel separated 1a, 1, and 1b, eluting with n-hexane, n-hexane–diethyl ether (30:1), and n-hexane–diethyl ether (10:1), respectively. They were characterized by MS and ¹H and ¹³C NMR (Table VIII). In addition, 1b shows the ester carbonyl absorption band at 1770 cm⁻¹ in its IR spectrum and on hydrolysis yields 2-(4-ethoxyphenyl)-2-methylpropanol (1f) and 3-phenoxybenzoic acid characterized by MS and ¹H NMR (for the methyl ester 1c). 1a and 1b are formed in about equal amounts on photolysis in methanol or acetonitrile–water in the presence of oxygen. Both 1a and 1b seem to be more photostable than 1 and are enriched during solution photolysis.

Further photodecomposition of 1 and its primary photoproducts in solution leads to a complex degradation mixture arising from the ethoxyphenyl (1d,f) and phenoxyphenyl (1c,e,g–i) moieties.

Photoproducts of 2 (Figure 3; Table IV). Photolysis in oxygenated methanol results in two major products, 3-[4-(4-ethoxyphenyl)-4-methylpentyl]dibenzofuran (2a) and 1-(4-fluorophenyl)-4-(4-ethoxyphenyl)-4-methylpentane (2b), identified by GC-MS. The dibenzofuran ring system of 2a is very stable on photolysis in methanol at λ > 290 nm with yields higher than 70% based on decomposition of the parent compound. Photodecomposition is very slow as a thin film at 290–320 nm, yielding only small amounts of 2a and no detectable 2b.

Photoproducts of 3 (Figures 4 and 5; Table V). Irradiation of 3 in oxygenated methanol results in a complex mixture of more than 50 photoproducts detected by GC-FID and GC-MS, with most of these products eluting just before or after 3 itself, consistent with their retaining the basic structure of the parent compound. The ion chromatogram of m/e 392 features two signals at prolonged

Table V. GC and MS Characteristics of NRDC 199 (3) and Some of Its Photoproducts

compd	R_t,[a] min	m/e (relative intensity)[b]	
		M+	important fragments
3	61.1	378 (5, Cl)	201 (20), 181 (10), 177 (100, Cl), 142 (20), 115 (20)
3a/b	62.9	392 (30, Cl)	241 (100), 239 (80), 207 (80, Cl), 181 (30), 177 (80, Cl), 142 (30), 115 (20)
3a/b	64.7	392 (20, Cl)	241 (40), 227 (20), 181 (20), 177 (100, Cl), 142 (30), 115 (20)
3c	9.2	154 (30, Cl)	139 (100, Cl), 111 (60, Cl)
3d	10.2	170 (30, Cl)	139 (100, Cl), 111 (60, Cl)
3e	12.4	166 (30, Cl)	139 (100, Cl), 111 (50, Cl)
3f	16.3	180 (60, Cl)	151 (20, Cl), 117 (70), 116 (70), 115 (100)
3g	20.0	210 (40, Cl)	151 (50, Cl), 116 (60), 115 (100)
3h	20.1	202 (100)	181 (10), 159 (20), 115 (20), 109 (20)
3i	20.4	198 (10, Cl)	183 (5, Cl), 166 (10, Cl), 139 (100, Cl), 111 (40, Cl)
3j	25.9	216 (100)	215 (50), 199 (20), 187 (30), 159 (20)
3k	29.5	230 (100)	201 (80), 181 (90), 158 (10), 139 (20)
3l	30.8	246 (100)	215 (80), 187 (20), 158 (10), 139 (20)
3m	31.5	262 (20)	231 (100), 215 (10), 187 (5), 159 (5), 139 (5)
3n	33.5	260 (100)	201 (60), 181 (70), 107 (30)

[a] GC conditions given in Materials and Methods. See Figure 3. [b] Fragments containing chlorine are indicated.

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Table VI. GC and MS Characteristics of NRDC 200 (4) and Some of Its Photoproducts

compd[a]	R_t,[b] min	M+	important fragments
			m/e (relative intensity)
4	26.4	388 (5)	201 (5), 187 (100), 181 (10), 159 (20)
4c	10.1	164 (30)	149 (60), 121 (100)
4d	10.5	180 (20)	149 (20), 121 (100)
4i	14.0	208 (20)	177 (10), 149 (100), 121 (100)

[a] Additional photoproducts from the phenoxyfluorophenyl moiety identical with those obtained from **3** are designated with asterisks in Figure 5. [b] GC conditions given in Materials and Methods.

Table VII. Important Fragments and Fragmentation Series in MS Analysis of 1-4 and Some of Their Major Photoproducts

fragment (R+)	compds	fragmentation series (m/e)
$C_2H_5OC_6H_4C(CH_3)_2$	1, 1a,b,d,f, 2, 2a,b	163, 135, 107
$C_6H_5OC_6H_4CH_2$	1, 1a	183
$C_6H_5OC_6H_4CO$	1b,c,g,i	197
$C_6H_5OC_6H_4$	1c,e,i	169, 141, 115
$C_6H_5OC_6H_4C$	1g,h	181, 169, 141, 115
$C_6H_5OC_6H_3FCH_2$	2-4	201, 181
$C_6H_4OC_6H_3CH_2$	2a, 3a/b,h,k,n	181
$C_6H_4FCH_2$	2b	109
$ClC_6H_4C_5H_6$	3, 3a/b	177 (Cl), 142, 115
ClC_6H_4CO	3c–e,i	139 (Cl), 111 (Cl)
$ClC_6H_4C_3H_4$	3f,g	151 (Cl), 117, 116, 115
$C_6H_5OC_6H_4FCO$	3j,l,m	215
$C_2H_5OC_6H_4C_5H_6$	4	187, 159
$C_2H_5OC_6H_4CO$	4c,d,i	149, 121

R_t consistent with the tentative structures **3a/b** but not fully supported by their fragmentation patterns, which undoubtedly contain a major contribution from other inadequately resolved photoproducts. Other products exhibit masses (m/e) appropriate for photoisomerization (378) and for addition of methanol (410). Further compounds in the R_t range of **3** show molecular ions of m/e 394. Epoxides of **3** are not detected. Additional high molecular weight products are evident on derivatizing the photolysate with diazomethane, indicating that some acidic products retain much of the original molecular structure.

Photolysis in oxygenated methanol leads to considerable cleavage of **3** since some of the products (e.g., **3c–n**) have one but not both of the 4-chlorophenyl and 3-phenoxy-4-fluorophenyl moieties. In some of these products (**3d,e,i**) the cyclopropyl ring is lost, showing that this is one possible site of oxidation.

Photolysis in methanol excluding oxygen results in fewer breakdown products and a higher percentage of compounds eluting in the R_t range of **3**. Rose bengal sensitized photooxidation of **3** in oxygenated methanol is very slow with <5% reaction within 50 h, giving a variety of products again eluting in the R_t range of the parent compound.

Photolyses of 4 (Figure 5; Table VI). The pattern of photoproducts for **4** in oxygenated methanol is generally

similar to that for **3** with several major GC peaks in the R_t region of **4** itself. In contrast to **4**, three major photoproducts exhibit quite intense molecular ions at m/e 388 and fragmentation patterns similar to those of **4** consistent with their being more stable photoisomers. Other major compounds are substitution or addition products of methanol featuring molecular masses of m/e 418 and 420 and MS base peaks different from those of **4**. The 4-ethoxyphenyl and 3-phenoxy-4-fluorophenyl moieties remain mostly untouched, but the cyclopropyl ring is sometimes lost to yield products with a carbonyl group (**4c,d,i**).

Toxicity of 1 and Its Major Photoproducts (Table X). The two major identified photoproducts of **1** are considerably less toxic than **1** itself to houseflies and goldfish.

DISCUSSION

Pyrethroid photochemistry is well understood for compounds with ester or oxime ether central linkages (Brown and Casida, 1984; Brown et al., 1983; Ruzo, 1983a,b). These relatively photosensitive substituents are replaced in pyrethroids 1-4 by central linkages of widely varying photostability, e.g. as thin films alkane > ether > alkene. The identified or proposed photoproducts are formed by photolysis of only the central linkage for ether **1** and alkenes **3** and **4** and of only the 3-phenoxy-4-fluorophenyl moiety of alkane **2** consistent with their chromophores and overall photoreactivities. Loss of the ethoxy moiety is not observed with any of the compounds and of the phenoxy moiety only with **2** where other reactions are largely precluded. The identified photoproducts from cleavage of the central linkage also retain the ethoxy and phenoxy substituents, further indicating that these are not particularly photosensitive sites.

Photodegradation of **1** with an ether central linkage is initiated by formation of radical intermediates either as a pair (A) or by radical abstraction (B), leading to two independently formed major photoproducts **1a** and **1b** (Figure 2). Generation of **1a** is limited to photolysis in solution, leading to the proposed mechanism of excitation of **1**, cleavage of the O–CH_2 bond, extrusion of CH_2O, and formation of two rather stable radicals (pair A) in a solvent cage, which recombine to give **1a** that is quite resistant to further decomposition. This is probably not a concerted process since **1a** is not observed in thin-film irradiations. Formation of **1b** requires oxygen and is not limited to photolysis in solution, consistent with abstraction of hydrogen to give radical B, reaction with oxygen to form hydroperoxide C, and dehydration to yield ester **1b**. An alternative mechanism of benzylic oxidation is initiated by electron transfer from the ether to oxygen, resulting in superoxide and an ether radical cation that can further react to give C and **1b**. In any case, **1b** appears to be a major photoproduct on exposure of **1** as oxygenated solutions or thin films to light under environmental type conditions. Further degradation of intermediate species leads to minor products (**1c–i**) retaining the ethoxy or

Table VIII. ¹H and ¹³C NMR Spectral Characteristics of Ethofenprox (1) and Its Two Major photoproducts

compd	chemical shifts, δ
	¹H NMR
1	1.30 (s, $(CH_3)_2C$), 1.39 (t, CH_3CH_2), 3.40 (s, CCH_2O), 4.00 (q, CH_3CH_2), 4.44 (s, OCH_2Ar), 6.8–7.3 (m, Ar)
1a	1.29 (s, $(CH_3)_2C$), 1.40 (t, CH_3CH_2), 2.80 (s, CCH_2Ar), 3.98 (q, CH_3CH_2), 6.4–7.3 (m, Ar)
1b	1.37 (t, CH_3CH_2), 1.40 (s, $(CH_3)_2C$), 4.00 (q, CH_3CH_2), 4.28 (s, CCH_2O), 6.8–7.7 (m, Ar)
	¹³C NMR
1	14.92 (CH_3CH_2), 26.14 (CH_3C), 38.51 (C), 63.33 (CH_3CH_2), 72.75 (OCH_2Ar),[a] 80.30 (CCH_2O),[a] 114–158 (Ar)
1a	14.94 (CH_3CH_2), 28.54 (CH_3C), 38.42 (C), 51.09 (CCH_2Ar), 63.29 (CH_3CH_2), 114–158 (Ar)
1b	14.88 (CH_3CH_2), 25.96 (CH_3C), 37.82 (C), 63.33 (CH_3CH_2), 73.81 (CCH_2O), 165.82 (CO), 114–158 (Ar)

[a] Determined by ¹H–¹³C long-range-correlated two-dimensional NMR spectroscopy.

Pyrethroid Photochemistry

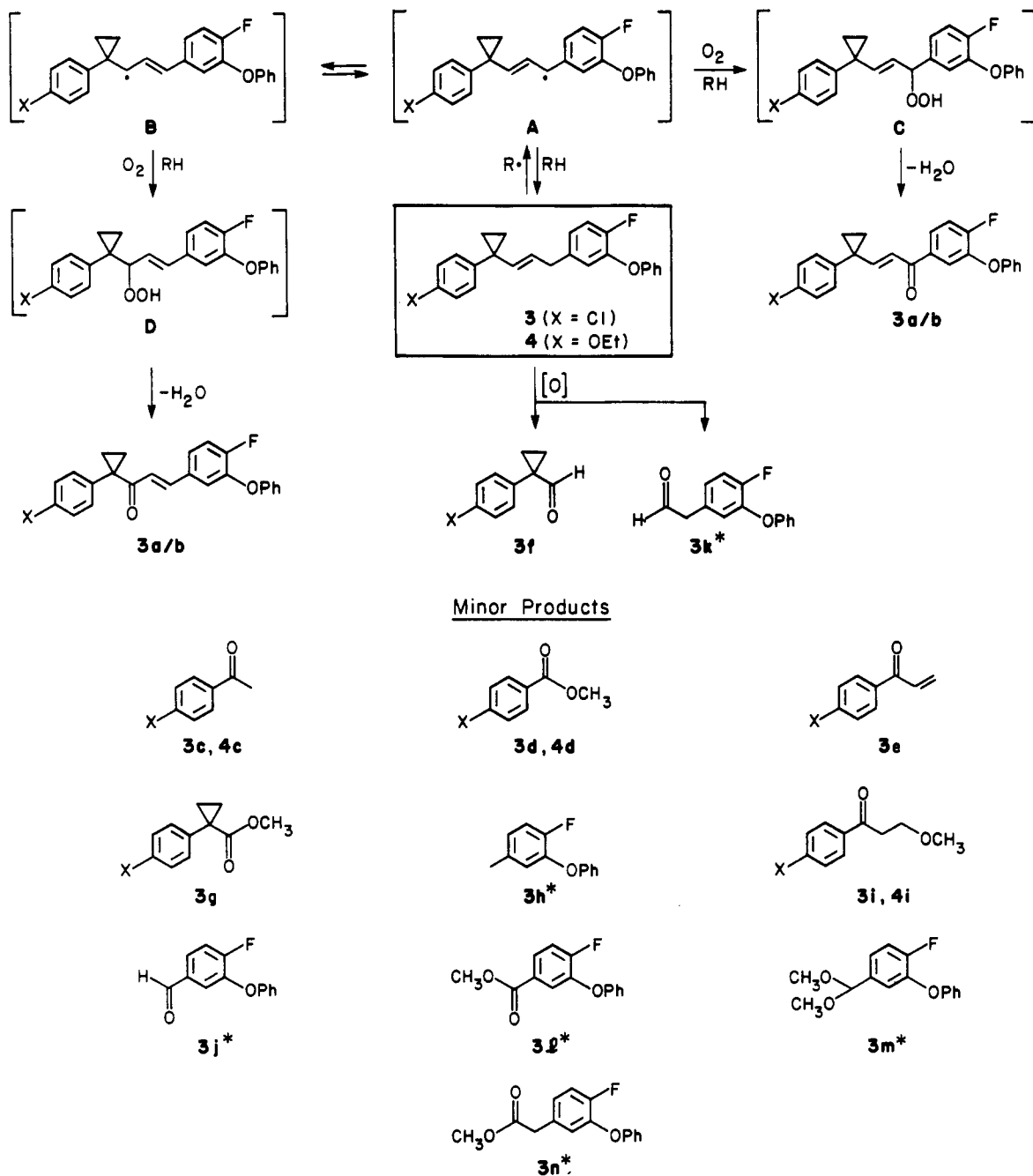*J. Agric. Food Chem.*, Vol. 37, No. 1, 1989 **221**

Figure 5. Tentative partial photodegradation pathways and minor photoproducts for NRDC 199 (**3**) and NRDC 200 (**4**) with alkene central linkages as methanol solutions. Photoproducts from the phenoxyfluorophenyl moiety of **4** identical with those obtained from **3** are designated by asterisks. RH is a hydrogen donor.

Table IX. Photochemical Yields for Ethofenprox (1) Irradiated in Solution and as a Thin Film at 290–320 nm

		photoproduct yield,[b] %			
compd	R_t,[a] min	MeOH/ N_2	MeOH/ O_2	CH_3CN/ H_2O/ O_2	thin film
1a	21.4	60	34	25	<3
1b	24.5	6	28	28	85
1c	13.8	<3	7	12	<3
1d	8.6	5	5	<3	<3
1e	9.8	<3	<3	<3	<3
1f	10.6	<3	7	<3	<3
1g	12.3	<3	<3	<3	<3
1h	13.3	<3	<3	<3	<3

[a] GC conditions given in Materials and Methods. [b] Yields are calculated as percent of total products with use of HRGC-FID for detection and under the assumption that the FID response of each product is similar to that of the parent. Irradiation for 50 h as solutions and 4 h as thin films giving 20–50% reaction.

Table X. Toxicity of Ethofenprox (1) and Two Major Photoproducts to Houseflies and Goldfish

	housefly LD_{50}, $\mu g/g$		goldfish
compd	unsynergized	piperonyl butoxide	LC_{50}, ppm
1	1	0.1	3.5[a]
1a	10	60	>5[b]
1b	125	>500	>7[b]

[a] Udagawa (1986) reports a 48-h threshold limit for mortality of 1.7 ppm. [b] No toxic effects at indicated concentrations.

phenoxy moieties. Photodecomposition appears to be a detoxification process since **1a** and **1b** are much less toxic than **1** to houseflies and goldfish.

Pyrethroid **2**, lacking a photosensitive central linkage, undergoes photoreaction via excited intermediate **A** (presumably by elimination of hydrogen fluoride as in the case of other haloaromatic cyclizations; Letcher and Wong,

1977) to give dibenzofuran derivative **2a** and via radical pair **B** to form fluorophenyl derivative **2b**, both of which appear to be very stable photoproducts (Figure 3).

Only a few of the multitude of photoproducts of **3** and **4** are tentatively characterized (Figure 5). Reactivity is centered at the allylic position involving radical formation (**A**) followed by rearrangement (**B**). Either radical **A** or **B** can react with oxygen (through hydroperoxides **C** and **D**) to yield products tentatively identified as the α,β-unsaturated ketones **3a/b**. Additional photoproducts arise from isomerization and reaction with methanol based on their GC–MS characteristics. Although not shown in Figure 5, isomerization may proceed by hydrogen abstraction from **A** to give (*Z*)-**3** or (*Z*)-**4** and from **B** to give the corresponding positional isomers. Isomers may also arise from rupture of the cyclopropane ring and subsequent cyclization. Methanol addition to these radical intermediates can give rise to the observed (but unidentified) products, which incorporate either 30 or 32 amu. Oxidative cleavage of the double bond gives rise to a plethora of products (Figure 5), some of which are common to both **3** and **4**, i.e. those formed from the phenoxyfluorophenyl moiety.

In summary, a variety of central linkages, including ester, ether, alkane, and alkene, confer pyrethroid-like insecticidal activity. The nature of the central linkage also determines the degree of photostability and the type and variety of photoproducts formed.

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Hydroxycineole: Four New Metabolites of 1,8-Cineole in Rabbits

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The metabolites of 1,8-cineole in rabbit urine were isolated by preparative gas chromatography. With the aid of mass spectra, ¹H NMR spectra, ¹³C NMR spectra, and infrared spectra, major metabolite **2** has been established as 2-*exo*-hydroxycineole, metabolite **3** as 2-*endo*-hydroxycineole, metabolite **4** as 3-*exo*-hydroxycineole, and metabolite **5** as 3-*endo*-hydroxycineole. Bioavailability was examined from blood levels of unchanged cineole and metabolites following oral dosing.

1,8-Cineole (**1**), eukalyptol, is a main constituent of essential oil from *Eucalyptus polybractea*, a component of a drug for urolithiasis. 1,8-Cineole and essential oils

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containing 1,8-cineole are used extensively in the food and cosmetic industries. Until recently, however, little was known about the metabolism of this terpene in mammals. It is known that 1,8-cineole is converted to oxidized products, 9-hydroxycineole and cineol-9-oic acid, by an enzyme of metabolism in brushtail possum (*Trichosurus vulpecula*) (Southwell et al., 1980; Flynn and Southwell, 1979). The aim of this study is to clarify natural smell substance biotransformation in animal biochemistry. The metabolism of α-pinene, β-pinene, pinane, 3-carene, carane,