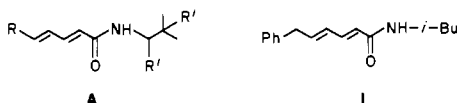


Photochemistry of the Prototype Insecticide (2*E*,4*E*)-*N*-Isobutyl-6-phenylhexa-2,4-dienamide

Luis O. Ruzo,* Stephen J. Holloway,¹ John E. Casida, and V. V. Krishnamurthy

The photochemical reactions of the prototype compound (2*E*,4*E*)-*N*-isobutyl-6-phenylhexa-2,4-dienamide (1) are examined as a first step in understanding the environmental degradation of a potentially important class of insecticides. The reaction rate of 1 in aerated methanol irradiated at 310 and 360 nm is similar to that of cypermethrin, a relatively photostable pyrethroid insecticide. The predominant process on direct or sensitized photolysis is *E/Z* isomerization with the isomer ratio at equilibrium being 2*E*,4*E* > 2*Z*,4*E* > 2*E*,4*Z* > 2*Z*,4*Z*. On irradiation of 1 in ethanol with benzophenone, the allylic radicals derived from 1 retain their *trans* geometry during coupling with ethanol-derived radicals. Other photoproducts retaining the isobutylamide moiety are the 4,5-epoxide of 1, the aldehyde from cleavage of the 4,5 double bond, and *N*-isobutylmaleimide. Photooxidation also yields phenylacetaldehyde in major amounts and trace levels of (2*E*)-4-phenylbut-2-enal and benzaldehyde. The identified photoisomerization and photooxidation reactions of 1 are probably detoxification processes.

The need to develop new types of insecticides has led to continuing research on natural and synthetic isobutylamides and related lipid amides. The (2*E*,4*E*)-dienamide structural requirements common to the most active compounds (A: R = a variety of substituents; R' = H,



CH₃) (Jacobson, 1971; Miyakado et al., 1985a,b; Su, 1985; Elliott, 1985; Elliott et al., 1986) are illustrated by 1 (Ph = phenyl, *i*-Bu = isobutyl) as a simple prototype compound for structural optimization (Elliott, 1985; Elliott et al., 1986). Isobutylamide 1 also provides a suitable starting point for studies on environmental stability and photo-reactions of the toxophoric moiety. The present investigation evaluates the photochemical fate of 1 as background for optimizing and understanding this potential new class of insecticides.

MATERIALS AND METHODS

Chromatography. Thin-layer chromatography (TLC) employed silica gel F-254 chromatoplates (0.25 mm, EM Reagents) with solvents as specified and product recovery from the gel by sonication in chloroform or methanol. Gas chromatography (GC) utilized a 3% SP 2100 column (1 m, 3 mm (i.d.), Supelco) operated at 30 mL/min with argon-methane (19:1) isothermally at 190 °C (1 and its photoproducts) or 220 °C (cypermethrin). The coupled GC-mass spectrometry (MS) system involved a 5840 Hewlett-Packard GC with a 10-m high-performance methyl silicone capillary column (80–240 °C, 20 °C/min; helium carrier gas at 1 mL/min). Retention times (*R_t*) are reported in minutes.

Spectroscopy. Ultraviolet (UV) spectra were obtained on a Perkin-Elmer 576 ST spectrophotometer with methanol solutions of 1 (3.3 mM) and cypermethrin (15 mM). MS utilized a Hewlett-Packard 5985B instrument operated under electron impact (EI) or chemical ionization

(CI) conditions at 70 and 230 eV, respectively. CI was carried out with methane (0.8 Torr) as the ionization gas. Molecular ions (EI, M⁺), quasi-molecular ions (CI, MH⁺), and significant fragments are reported as *m/z* units, with relative intensities given in parentheses (Table II). In CI-MS all ions incorporating C₂H₅ (M + 29) and C₃H₅ (M + 41) were observed with approximate intensities of 15 and 5%, respectively. Nuclear magnetic resonance (NMR) spectra were recorded with a Bruker WM 300 NMR spectrometer at 300-MHz ¹H operating frequency in chloroform-*d*. Chemical shifts are reported (ppm) downfield from tetramethylsilane, and the coupling constants are reported in hertz. Individual proton assignments were made mostly on the basis of chemical shifts and coupling constants, but in some cases homonuclear decoupling experiments and *J*-resolved 2D NMR experiments (Aue et al., 1976) were used for identification of multiplet patterns.

Chemicals. Designations for 1, its isomers (2–4), and other photoproducts (5–10) are given in Figure 1. Dienamide 1 was prepared by the Wittig reaction between (2*E*)-4-phenylbut-2-enal (9) [synthesized from phenylacetaldehyde (6)] and the ylide prepared from (*N*-isobutylcarboxamido)methylenediphenylphosphonium bromide (Figure 2). The product was purified by TLC (silica gel; ethyl acetate-hexane, 3:7) and recrystallized from methanol (mp 119–121 °C).

Treatment of 1 (1 mg) with 1 equiv of *m*-chloroperbenzoic acid (MCPBA) in chloroform (1 mL) for 1 h yields two isomers in a 5:1 ratio (integration of the olefinic and epoxide proton resonances in the NMR spectrum). The major isomer (86%) designated as 5 arises from epoxidation of the 4,5 double bond and the minor one (14%) from oxidation of the 2,3 double bond (Table I). The magnitude of the coupling constants indicates that the double bond and the epoxide are in the *trans* configuration in both isomers.

Irradiation Procedures. Samples were photolyzed at 35–40 °C in a Rayonet photoreactor (The Southern New England UV Co., Middletown, CT) equipped with 16 3500 or 3000 RPR lamps with peak outputs at 360 and 310 nm, respectively. Solutions (1 mL) were contained in sealed borosilicate tubes held in a merry-go-round arrangement. Irradiations were typically for 1 and 30 h at 310 and 360 nm, respectively. Photolyses were carried out in hexane, cyclohexane, methanol, ethanol, and aqueous acetonitrile. Solutions were aerated by bubbling oxygen through (1 h) or deoxygenated with bubbling nitrogen. Sunlight pho-

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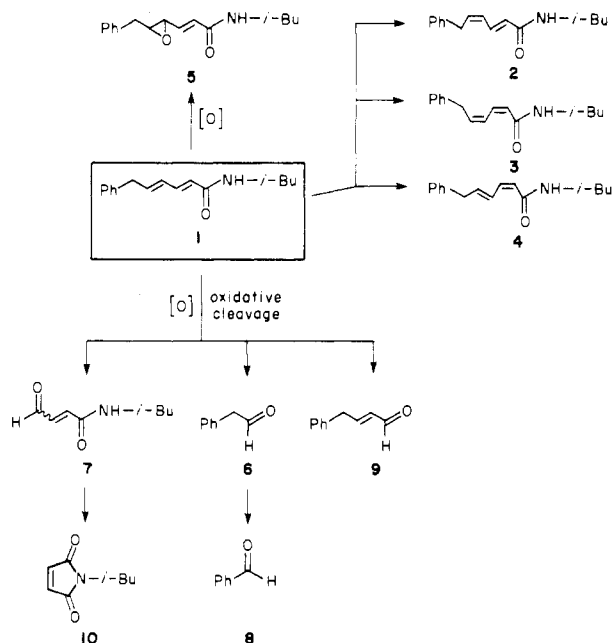


Figure 1. Photoisomerization and photooxidation reactions of 1.

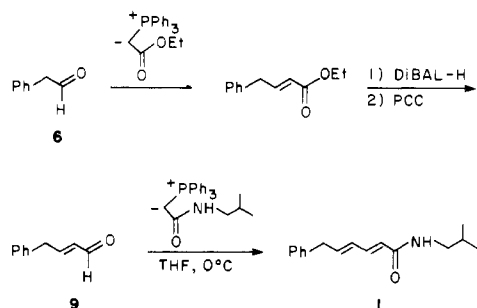


Figure 2. Synthesis of 1: DIBAL-H = diisobutylaluminum hydride; PCC = pyridinium chlorochromate; THF = tetrahydrofuran.

tolysis of 1 in solution (1.6 mM in methanol) or as a thin film ($3 \mu\text{g}/\text{cm}^2$) on glass covered with quartz was carried out for 6 days (Berkeley, November).

To examine sensitized photolysis, deoxygenated benzene solutions of 1 (8.2 mM) were irradiated at specified wavelengths (Table III) in the presence of a 10-fold molar excess of the sensitizer (J. T. Baker, Phillipsburg, NJ). Isomeric composition as percent of isomer mixture (Table III) was determined from the total ion current of GC-MS peaks. In one case ethanol solutions of 1 (8 mM) and benzophenone (20 mM) were utilized to examine radical addition to the isobutylamide.

Photolysates were routinely monitored by GC-MS and TLC. Individual products were isolated by TLC and characterized by NMR and MS and where possible by cochromatography and spectroscopic comparison with authentic standards (Tables I and II). Quantitations (GC-MS) relied on benzophenone as the internal standard. Reaction rates were determined from three separate irradiation time periods for 1 and (1*R*,*cis*, α *S*)-cypermethrin (Roussel UCLAF, Paris, France).

RESULTS AND DISCUSSION

Reaction Rates of 1 and Cypermethrin. Molar extinction coefficients ($M^{-1} \text{cm}^{-1}$) are 364 for 1 at 300 nm but <1 at 360 nm and 11 for cypermethrin at 300 nm. In order to directly relate their reactivities, aerated methanol solutions of 1 (3.3 mM) and cypermethrin (31 mM) were irradiated at 310 and 360 nm. Reaction rate constants (k_r)

Table I. NMR Characteristics of Dienamide 1 and Its Isomers and Epoxides

isomer no.	R_f^a	a	b	c	d	e	f	g	h	i	
2 <i>E</i> ,4 <i>E</i>	1	0.35	0.92 ($J_{ab} = 6.4$)	1.79 ($J_{bc} = 6.4$)	3.1 ($J_{cd} = 6.4$)	5.56	5.79 ($J_{ef} = 15.1$)	nd ^d	6.17 ($J_{gh} = 14.9$, $J_{fg} = 9.4$)	6.20	3.48 ($J_{hi} = 7.0$)
2 <i>E</i> ,4 <i>Z</i>	2	0.40	0.95 ($J_{ab} = 6.4$)	1.80 ($J_{bc} = 6.4$)	3.20 ($J_{cd} = 6.4$)	5.60	5.91 ($J_{ef} = 14.8$, $J_{fg} = 11.4$)	7.70 ($J_{gh} = 14.8$, $J_{hi} = 11.2$)	5.91 ($J_{gh} = 11.2$, $J_{hi} = 8.2$)	6.20 ($J_{fg} = 11.4$, $J_{gh} = 8.2$)	3.65 ($J_{hi} = 8.2$)
2 <i>Z</i> ,4 <i>Z</i>	3	0.46	0.94 ($J_{ab} = 6.5$)	1.80 ($J_{bc} = 6.5$)	3.20 ($J_{cd} = 6.2$)	5.56	5.68 ($J_{ef} = 11.5$, $J_{fg} = 11.5$)	6.86 ($J_{ef} = 11.5$, $J_{gh} = 9.5$)	5.95 ($J_{gh} = 9.5$, $J_{hi} = 9.2$)	7.43 ($J_{fg} = 11.5$, $J_{gh} = 9.5$)	3.60 ($J_{hi} = 9.2$)
2 <i>Z</i> ,4 <i>E</i>	4	0.52	0.93 ($J_{ab} = 6.4$)	1.80 ($J_{bc} = 6.4$)	3.15 ($J_{cd} = 6.4$)	5.54	5.51 ($J_{ef} = 11.4$, $J_{fg} = 11.4$)	6.39 ($J_{ef} = 11.4$, $J_{gh} = 15.0$)	7.59 ($J_{ef} = 11.4$, $J_{hi} = 7.3$)	6.05 ($J_{gh} = 15.0$, $J_{hi} = 7.3$)	3.50 ($J_{hi} = 7.3$)
2,3-epoxide			0.92 ($J_{ab} = 7$)	1.80 ($J_{bc} = 6.7$)	3.08 ($J_{cd} = 6.7$)	5.53					3.41
											6.16 ($J_{hi} = 6.7$)
4,5-epoxide	5		0.92 ($J_{ab} = 7$)	1.80 ($J_{bc} = 6.4$)	3.16 ($J_{cd} = 6.4$)	5.53	6.08 ($J_{ef} = 15.1$)	6.67 ($J_{fg} = 6.4$)	3.29 ($J_{gh} = 2.0$)	3.11 ($J_{hi} = 5.4$)	2.94 (AB q, $^2J = 14.7$)

^aTwo developments with acetone-cyclohexane-ethyl acetate, 1:2:8. ^b $\delta \pm 0.05$ ppm. ^c $J \pm 0.1$ Hz, long-range coupling not detected in all cases. ^dOverlaps with aromatics.

Table II. GC-MS Characteristics of Photoproducts from Irradiation of 1 in Oxygenated Methanol at 360 nm

photoproduct designation	R_t , min	mass spectral data	
		EI	CI
2	8.3	243 (26), 171 (42), 152 (52), 143 (88), 128 (100), 91 (48)	244 (100)
3	8.1	243 (22), 171 (46), 152 (58), 143 (90), 128 (100), 91 (40)	244 (100)
4	7.9	243 (5), 171 (8), 152 (100), 128 (22), 91 (12)	244 (100)
5	7.4	259 (8), 231 (15), 159 (60), 91 (100)	250 (100)
6	1.6	120 (22), 91 (100)	121 (100)
7	3.7	155 (32), 112 (100), 83 (79)	156 (100)
8	1.2	106 (100)	107 (100)
9	3.1	132 (85), 131 (100), 105 (62)	133 (100), 119 (18), 105 (21)
10	2.0	153 (46), 110 (100)	154 (100), 121 (31)

Table III. Effect of Selected Sensitizers on the E/Z Photoisomerization of 1 in Benzene Solution^a

sensitizer	E_t^b	isomer yield, %			
		1	2	3	4
anthracene	42	96	<1	<1	3
7H-benz[de]anthracen-7-one	47	98	<1	<1	<1
benzil	54	58	4	<1	37
1'-acetonaphthone	56	58	15	2	25
biphenyl	65	69	10	<1	21
benzophenone	69	59	17	3	21
none		98	<1	<1	1

^aIrradiation for 2 h at 360 nm except in the case of biphenyl (7 h, 300 nm). ^bTriplet energy, kilocalories/mole.

were similar for both substrates: 1.2–1.4 mM h⁻¹ (310 nm) and 0.10–0.15 mM h⁻¹ (360 nm). These values were measured at intervals between 10 and 40% conversion when major products (see below) consist almost entirely of E/Z isomerized materials.

Photoproducts on Direct Photolysis. The identity (Figure 1) and distribution of photoproducts from 1 on direct irradiation are similar in all solvents studied and on irradiation by UV or sunlight. On exclusion of oxygen from the irradiated solutions only 2–4 are observed on photolysis. Even in the presence of oxygen the predominant process is E/Z isomerization of the dienamide group. For example, photolysis of 1 (1.4 mM) in methanol (23 h, 360 nm) results in 42% reaction. GC-MS reveals formation of the 2*E*,4*Z* (2, 12%), 2*Z*,4*Z* (3, 3%), and 2*Z*,4*E* (4, 56%) isomers, characterized by NMR and EI- and CI-MS after TLC (cyclohexane–ethyl acetate–acetone, 8:2:1, two developments) separation of the isomers (Table I). Additional products formed (Table II; Figure 1) are characterized by GC-EI-MS and GC-CI-MS (5–10) and by GC cochromatography (5, 6, 8, 9). The 2,3-epoxide of 1 is not detected. The major of these products is phenylacet-aldehyde (6) formed in approximately 10% yield. Photolysis by sunlight as a thin film (15% reaction) results in conversion of 1 to the E,Z isomers, but the major products in this case include 6 and 10 while 5 is detected only as a trace component. Products 7 and 10 are only tentatively characterized by EI- and CI-MS.

Photoproducts on Sensitization. A series of triplet sensitizers ranging in triplet energies (E_t) from 42 to 69 kcal/mol were utilized to determine an approximate E_t for 1 (Table III). Irradiation at 360 nm in deaerated benzene reached a photostationary state after 2 h at which time the relative percent composition of 1–4 in the photolysate was determined (Table III). In all cases the isomer yields are in the order 2*E*,4*E* > 2*Z*,4*E* > 2*E*,4*Z* > 2*Z*,4*Z* and the E_t of 1 falls in the range of 48–53 kcal/mol (Table III).

Products not found in other systems are detected when benzophenone (30 mM) sensitization of 1 (8 mM) is carried out in ethanol solution (360 nm, 1 h). They have GC-MS R_t values of 8.7 and 9.0 min and are of reduced R_f on TLC (acetone–hexane, 3:5). J -Resolved 2D NMR of the isolated materials indicates the presence of products from 1,2- and

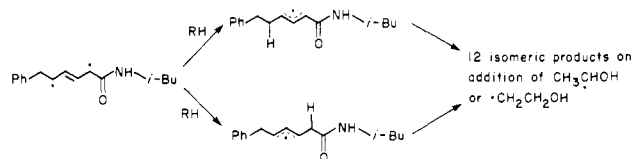


Figure 3. Possible radical intermediates in the sensitized photolysis of 1 in ethanol.

1,4-addition of hydrogen and C₁ or C₂ ethanol free radical to the 2 and 4 double bonds of 1. In principle, hydrogen abstraction by the diradical followed by trapping of the C₁ and C₂ ethanol free radicals by the allylic radical would generate 12 different isomeric products (Figure 3), i.e., four diastereomeric pairs from C₁ ethanol addition and four isomers from C₂ ethanol addition. Careful analysis of the vinylic and the aromatic region of the 2D NMR spectrum reveals 11 different trans vinylic protons of the type RCH=CHCHRR, all of them appearing as a doublet of doublets ($J = 15, 8$ Hz). No evidence was observed for the corresponding cis vinylic protons. Thus, the allylic radical retains the trans geometry during the coupling with ethanol-derived radicals. One other product (MH⁺, 246, R_t 7.0 min) is detected in benzophenone-sensitized photolyses that may arise from photoreduction of 1 by benzhydrol produced on reduction of benzophenone or by H abstraction from the solvent. Thus, the 1,2- and 1,4-diradicals from triplet sensitization are fairly long-lived intermediates as evidenced by the ease with which H abstraction takes place in the presence of a hydrogen source such as ethanol and by the formation of a reduced product from 1. In contrast, the 1,3-diradical formed on irradiation of cyclopropanecarboxylate pyrethroids cyclizes rather than undergo solvent addition or photoreduction (Ruzo, 1983).

Concluding Comments. The photostability of isobutylamide 1 is comparable to that of cypermethrin in solution, suggesting that direct irradiation may not be an important degradation pathway. Although 1 reacts to form isomers insecticidally inactive (Elliott, 1985), the most thermodynamically stable 2*E*,4*E* isomer is also the most insecticidal. On exposure to oxygen the dienamide system fragments to aldehydes that undergo further reaction (Figure 1). Structural modifications for photostabilization of this potential new class of insecticides might therefore emphasize (a) suitable replacements for the dienamide system that retain insecticidal activity but of decreased sensitivity to photooxidation and (b) aromatic or other substituents of appropriate triplet energy to act either as sensitizers favoring the insecticidal isomer or as energy acceptors to modify or decrease the isomerization process.

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100-52-7; 9, 55177-35-0; 10, 4120-68-7; anthracene, 120-12-7; 7H-benz[de]anthracen-7-one, 82-05-3; benzil, 134-81-6; 1'-acetonaphthone, 941-98-0; biphenyl, 92-52-4; benzophenone, 119-61-9.

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Hydrolytic and Photolytic Degradation of Flurochloridone

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Hydrolytic and photolytic studies of flurochloridone, 3-chloro-4-(chloromethyl)-1-[3-(trifluoromethyl)phenyl]-2-pyrrolidinone, have been completed in buffered aqueous solutions. Flurochloridone hydrolysis rates were measured as a function of pH at 25 and 40 °C. No hydrolysis occurred at pH 5, 7, or 9 at 25 °C or at pH 5 at 40 °C. Appreciable hydrolysis occurred under the remaining conditions; at 40 °C at pH 7 and 9 the observed half-lives were 190 and 140 days, respectively. Five hydrolytic degradation products were identified. Analysis of radioactivity indicated that approximately 96% of the radiocarbon was recovered. Photolysis rates were measured at pH 7 at 25 °C, conditions under which negligible hydrolysis occurred. The pseudo-first-order photolytic half-life was 4.3 days. Six photolytic degradation products were identified. Analysis of radioactivity accounted for 83% of the initial radiocarbon.

Flurochloridone, 3-chloro-4-(chloromethyl)-1-[3-(trifluoromethyl)phenyl]-2-pyrrolidinone (1), is a selective herbicide reported to reduce chlorophyll and carotenoid production in wheat (*Triticum aestivum* var. L. Mericopa) and corn (*Zea mays* var. L. Merit) (Devlin et al., 1979). The herbicide mode of action of flurochloridone was reported by Lay and Niland (1983) and Lay et al. (1985).

The present investigation was undertaken to study the hydrolysis and photolysis processes of flurochloridone and characterize the corresponding degradation products. The information developed in this study will aid in understanding the behavior of the compound in the environment.

EXPERIMENTAL SECTION

Chemicals. Flurochloridone and [3-¹⁴C]flurochloridone were produced by Stauffer Chemical Co., Richmond, CA. Technical flurochloridone typically consists of 3 parts trans isomer and 1 part cis isomer. The structural assignment of the isomeric components was reported earlier (Tseng and Gless, 1983). Radiolabeled flurochloridone, with a specific activity 8.5 mCi/mM, was purified by TLC using ethyl ether-pentane (1:3, v/v) as the developing solvent to give a radiopurity of 98%.

1,5-Dihydro-5-methoxy-4-methyl-1-[3-(trifluoromethyl)phenyl]pyrrol-2H-one. To a solution of 9.3 g (0.03 mol) of flurochloridone (1) in 150 mL of methanol was added dropwise 14.0 g of 25% sodium methoxide (0.065 mol) in methanol with stirring. The mixture was heated at 60 °C for 3 h, cooled, and filtered. The filtrate was concentrated to a brown oil on a rotary evaporator. The oil was redissolved in 100 mL of methylene chloride, washed with 50 mL of 0.5 M HCl followed by 50 mL of water, dried over anhydrous sodium sulfate, and concentrated. The resulting residue was purified by column chromatography using hexane-chloroform (1:1, v/v) and silica gel to give 4.1 g (50.3%) of white crystalline solid, mp 69-70 °C. Anal. Calcd for C₁₃H₁₂F₃NO₂: C, 57.57; H, 4.46; N, 5.16. Found: C, 57.74; H, 4.53; N, 5.18.

1,5-Dihydro-5-hydroxy-4-methyl-1-[3-(trifluoromethyl)phenyl]pyrrol-2H-one (2). A solution of 2.45 g of 1,5-dihydro-5-methoxy-4-methyl-1-[3-(trifluoromethyl)phenyl]pyrrol-2H-one in 8 mL of glacial acetic acid and 1 mL of 6 N hydrochloric acid was allowed to stand at room temperature until crystallization occurred (~3 days). The white crystals were collected, washed with water, and dried; mp 150-152 °C. Anal. Calcd for C₁₂H₁₀F₃NO₂: C, 56.03; H, 3.89; N, 5.45. Found: C, 56.13; H, 3.84; N, 5.52.

3-Methyl-1-[3-(trifluoromethyl)phenyl]maleimide. To a solution of 11.2 g (0.1 mol) of methylmaleic anhydride in 50 mL of acetic acid was added 16.1 g (0.1 mol) of

Stauffer Chemical Company, Western Research Center, Richmond, California 94804-0023. (Now part of the ICI group of companies.)