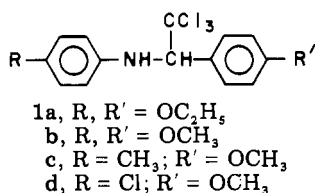


Controlling Photolability of *N*-(α -Trichloromethylbenzyl)aniline Insecticides

Gregory A. Yost and Larry L. Miller*

The products and relative rates of photolysis of *N*-(α -trichloromethyl-*p*-alkoxybenzyl)anilines were studied using 3:2 tetrahydrofuran-H₂O solutions and 3100-Å light. The 4-methoxy-, 4-methyl-, and 4-chloroaniline derivatives give similar products. The rate of the 4-methoxy is, however, much faster. A mechanism involving charge transfer from the aniline to the trichloromethyl group is proposed. The 2,4-dichloroaniline derivative also reacts slowly, but by a different pathway. This compound also has insecticidal activity.

N-(α -Trichloromethylbenzyl)anilines possess a combination of properties, which may make them a valuable new type of pesticide. Several members of this family of compounds show insecticidal activity which is quite comparable to some commonly used pesticides. For example, *N*-(α -trichloromethyl-*p*-ethoxybenzyl)-*p*-ethoxyaniline (**1a**) compared favorably with DDT, methoxychlor, and ethoxychlor in its toxicity to several target insects (Hirwe et al., 1972). Furthermore, this class of compounds



showed encouraging properties of biodegradability and low biological magnification when they were tested in a model ecosystem (Metcalf et al., 1971).

Studies on DDT photodecomposition, sensitized by *N,N*-diethylaniline (Miller et al., 1973), led to speculation that compounds like **1** would be photodegradable. Indeed, we have shown (Miller et al., 1974) that **1b** absorbs light in the solar region and readily photolyzes. Using 3100-Å light and a Pyrex filter, solutions or films of **1b** exposed to the air were completely reacted in a few hours. This strongly indicates that **1** will be degraded in the environment by photolysis. In fact, the utility of these compounds may be limited by their photolability. Our goal in the present research was to demonstrate a method for lengthening the lifetime and we report the results here.

EXPERIMENTAL SECTION

Instrumentation. A Bendix Model 2110 gas chromatograph equipped with a dual flame ionization detector was used with a 6 ft × 0.25 in. Teflon-lined aluminum column packed with 5% OV-1 on Chromosorb W. The operating conditions were: flow rate, 35 ml/min; injector port, 250 °C; detector, 300 °C; column temperature, for octyl chloride 85 °C, for decyl bromide 140 °C, and for DDT 220 °C.

High-Pressure Liquid Chromatography (HPLC). A Waters Associates ALC-202 liquid chromatograph with a differential uv detector operating at 254 nm was used. The column was 2 mm i.d. × 3 ft packed with Porasil A. The eluting solvent was 1:1 (v/v) diisopropyl ether-hexane. The column was operated at ambient temperature with a flow rate of 1.35 ml/min.

Nuclear Magnetic Resonance Spectra. All spectra were obtained on a Varian T-60 spectrometer. Chemical

shifts are reported as δ from tetramethylsilane internal standard.

Ultraviolet Spectra. Spectra were obtained on either a Cary 17 spectrometer or a Varian Model 635 spectrometer.

Infrared Spectra. All spectra were taken on a Beckman Acculab 3 ir spectrometer.

Mass Spectra. All spectra were taken on an AEI Model MS-12 spectrometer at 70 eV using a direct probe inlet.

Photolysis. A Rayonet photochemical reactor equipped with a merry-go-round and 16 lamps with major output near 310 nm was used. Sunlight photolyses were performed by placing samples in direct sunlight.

Pesticide Testing. Testing was performed by Dr. R. L. Metcalf at the University of Illinois, Urbana, Ill., using the screening methods established by the World Health Organization.

Cyclic Voltammetry. A PAR 373 potentiostat was used. A two-compartment cell was used to separate the reference electrode from the anode and cathode. The anode and cathode were platinum wires. The reference consisted of a silver wire dipped in an acetonitrile solution of AgNO₃ (0.1 M). The sweep rate was 0.2 V/s and the potential scanned from 0 to 2.0 V. The solvent was acetonitrile-0.1 M LiClO₄. All the oxidation processes were irreversible; therefore, the potentials quoted are kinetically controlled.

Synthesis. α -Trichloromethylbenzylanilines. These compounds were prepared by one of two procedures: (procedure A) the method of Hirwe et al. (1972) was used; (procedure B) a modification used to synthesize those compounds which gave poor yields by procedure A. The appropriate benzylideneaniline was mixed with 1.2 equiv of trichloroacetic acid without solvent in an Erlenmeyer flask. The flask was then placed in an oil bath which was slowly heated to 130 °C, and the reaction mixture was stirred frequently. The mixture was stirred at this temperature until all solid material had melted and the evolution of gas ceased. The reaction time was usually about 15 min. After allowing the mixture to cool to room temperature, it was dissolved in benzene and extracted with 2 N HCl. The resulting organic layer was then dried over Na₂SO₄ and then the solvent was removed under vacuum. If the desired product was a solid, the product mixture was dissolved in methanol and the product precipitated by evaporation to a small volume and cooling. If the desired product was a liquid or an oil, the product mixture was separated by chromatography on a column of activity grade I acidic Woelm alumina, eluting with hexane.

Several of these compounds (**1b**, **1c**, and **1d**) had been synthesized before (Hirwe et al., 1972) and the structures of these compounds were verified by comparison of their melting points and NMR spectra with published data: **1b**,

*Chemistry Department, Colorado State University, Fort Collins, Colorado 80521.

mp 110–111 °C (lit. mp 112 °C); **1c**, mp 84–85 °C (lit. mp 86 °C); **1d**, mp 96–97 °C (lit. mp 98 °C).

(α -Trichloromethyl-*p*-ethoxybenzyl)-2,4-dichloroaniline (**4**) was synthesized using method B in 54% yield. This compound is a viscous oil: ir (neat) 3420, 3000, 2960, 2890, 1630, 1600, and 1530 cm^{-1} ; NMR (CDCl_3) δ 1.34 (t, 3 H), 3.97 (q, 2 H), 4.99 (d, 1 H), 5.44 (d, 1 H), 6.3–7.2 (m, 7 H); mass spectrum m/e (relative intensity) 411 (4.3), 294 (100), 265 (19.7), 205 (18.3), 188 (15.9), 172 (18.3), 121 (13.6). Anal. Calcd: C, 46.5; H, 3.4; N, 3.4; Cl, 42.9. Found: C, 46.4; H, 3.5; N, 3.1; Cl, 42.9.

(α -Trichloromethyl-*p*-ethoxybenzyl)-4-chloro-2-trifluoromethylaniline (**5**) was also synthesized by method B in 48% yield and was also a viscous oil: ir (neat) 3460, 3000, 2955, 2890, 1620, 1580, and 1510 cm^{-1} ; NMR (CDCl_3) δ 1.46 (t, 3 H), 4.00 (q, 2 H), 5.04 (d, 1 H), 5.45 (br d, 1 H), 6.4–7.6 (m, 7 H); mass spectrum m/e (relative intensity) 446 (>1), 328 (100). Anal. Calcd: C, 45.7; H, 3.2; N, 3.3. Found: C, 45.8; H, 3.3; N, 3.0.

1,2-Bis(*p*-chlorophenyl)-3,3-dichloroaziridine was prepared by the method of Brooks et al. (1966). The product was a white powder: mp 149.5–150 °C; NMR (CDCl_3) δ 3.65 (s, 1 H), 7.02 (d, 2 H, $J = 8$ Hz), 7.38 (d, 2 H, $J = 8$ Hz), 7.45 (d, 2 H, $J = 8$ Hz); ir (KBr pellet) 1490, 1410, 1380, and 1262 cm^{-1} ; uv (tetrahydrofuran) max 228 (ϵ 13 400), 243 (ϵ 13 700), 278 (s) (ϵ 516).

Photolysis of *N*-(α -Trichloromethyl-*p*-methoxybenzyl)-*p*-methylaniline (**1c**). **1c** (400 mg) in 40 ml of tetrahydrofuran–water (60:40) was irradiated as described for **1b** (Miller et al., 1974) for 5 days. Acidic and basic products were isolated as described for DMA and yielded *p*-anisic acid (trace) and *p*-methylaniline (23%). The neutral products were separated by preparative TLC on 2 mm thick 20 \times 20 cm silica gel plates with fluorescent indicator (Brinkmann Instruments). The plates were eluted with 1:1 hexane–ether. After visualization the bands were scraped and extracted with tetrahydrofuran. The products found were *p*-anisaldehyde (13%) and a solid identified as *N*-(*p*-methylphenyl)-2-(*p*-methoxyphenyl)-2-hydroxyacetamide (47%): mp 141–142 °C; ir (KBr) 3290, 1660, 1645, 1620, and 1600 cm^{-1} ; NMR (CDCl_3) δ 2.33 (s, 3 H), 3.5 (br s, 1 H), 3.8 (s, 3 H), 5.18 (s, 1 H), 6.94 (d, 2 H), 7.16 (d, 2 H), 7.42 (d, 2 H), 7.44 (d, 2 H), 8.1 (br s, 1 H); mass spectrum m/e (relative intensity) 271 (10), 137 (100), 109 (20), 107 (18), 94 (10), 77 (19).

Photolysis of *N*-(α -Trichloromethyl-*p*-methoxybenzyl)-*p*-chloroaniline (**1d**). **1d** (0.400 g) in 40 ml of tetrahydrofuran–water (60:40) was irradiated for 5 days. A similar workup to the above yielded a trace of *p*-anisic acid and *p*-chloroaniline (27%). Preparative TLC on silica gel as described for **1c** gave *p*-anisaldehyde (13%) and a white solid (57%) which was identified as *N*-(*p*-chlorophenyl)-2-(*p*-methoxyphenyl)-2-hydroxyacetamide: ir (KBr) 3360, 3300, 1665, and 1580 cm^{-1} ; NMR (CDCl_3) δ 3.8 (s, 3 H), 5.22 (s, 1 H), 6.9–7.8 (m, 8 H), 8.2 (br s, 1 H); mass spectrum m/e (relative intensity) 291 (11), 137 (100), 109 (38), 94 (17), 77 (24).

Photolysis of *N*-(α -Trichloromethyl-*p*-ethoxybenzyl)-2,4-dichloroaniline (**4**). In 40 ml of tetrahydrofuran–water (60:40) 413 mg of **4** was irradiated for 70 h. After photolysis the product mixture was worked up as described above. Only a trace of *p*-ethoxybenzoic acid was detected and a similar amount of 2,4-dichloroaniline was found. The neutral fraction was subjected to preparative TLC on silica gel eluting with 9:1 hexane–ether. Visualization showed three major bands and several minor products. The three major bands were scraped and the material extracted with CH_2Cl_2 . Band 1 was shown to be unreacted

Table I. Uv Absorption Data for 1

Compd	λ_{max} (ϵ)	ϵ_{3100}
1b	3055 (1690)	1610
	2800 (2040)	
	2330 (18800)	
1c	2920 (sh) (2370)	960
	2810 (3310)	
	2720 (sh) (3560)	
	2410 (20640)	
1d	2970 (2330)	1760
	2800 (3690)	
	2480 (21400)	
4	3030 (2140)	1860
	2815 (1870)	
	2470 (17680)	
	2490 (26270)	
5	3110 (4400)	4400
	2810 (2460)	
	2490 (26270)	

4 (33%). Band 2 produced a viscous oil which was identified as *N*-(α -dichloromethyl-*p*-ethoxybenzyl)-2,4-dichloroaniline (**6**) (27%): ir (neat) 3420, 3370, 1730 (w), 1620, and 1600 cm^{-1} ; NMR (CDCl_3) δ 1.40 (t, 3 H), 3.98 (q, 2 H), 4.79 (d of d, 1 H, $J = 6.3$ Hz), 5.28 (d, 1 H, $J = 6$ Hz), 5.98 (d, 2 H, $J = 3$ Hz), 6.2–7.4 (m, 7 H); mass spectrum m/e (relative intensity) 377 (6.5), 294 (100), 266 (13), 217 (8.6), 189 (6.5), 172 (11), 154 (11). Band 3 gave a white solid which was identified as 2-(*p*-ethoxyphenyl)-3,5,7-trichloroindole (**7**) in 10% yield: mp 58–60 °C; ir (neat) 3430, 3320, and 1620 cm^{-1} ; NMR (CDCl_3) δ 1.44 (t, 3 H), 4.12 (q, 2 H), 6.96 (d, 2 H), 7.18 (d, 1 H), 7.54 (d, 1 H), 7.72 (d, 2 H), 8.2 (br s, 1 H); mass spectrum m/e (relative intensity) 339 (100), 310 (74), 295 (50). Anal. Calcd: C, 56.4; H, 3.5; N, 4.1. Found: C, 55.6; H, 3.6; N, 3.8.

Relative Rates of 1b, 1c, 1d, 4, and 5 in Sunlight. A thin film of DMA (4 mg) was formed by evaporating a tetrahydrofuran solution (2 ml) in each of two petri dishes. The same was done for each of the other compounds. One dish of each pair was placed in direct winter sunlight for 4 h. The other dish of each pair was kept as a control. After photolysis each plate was worked up as follows, and the control was likewise worked up without irradiation. The product mixture was washed from the dish with tetrahydrofuran and the volume of solvent was adjusted to 1 ml and four 10- μ l spots of this solution were placed at the origin of a 5 \times 10 cm silica gel TLC plate. The plate was then eluted with 1:1 hexane–ether and the spots corresponding to the starting material were scraped and shaken with tetrahydrofuran. This solution was adjusted to a volume of 3 ml and the uv spectrum of the mixture taken. The loss of starting material was determined by comparing the absorption of λ_{max} of the photolyzed sample to that of the control.

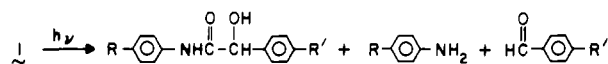
RESULTS

The rates of photochemical reactions are generally determined by the amount of light absorbed and the relative rates of product formation and deactivation from the excited state(s). One means of decreasing the lability is, therefore, to decrease the absorptivity of the molecule in the solar region. The absorption of solar light by α -trichloromethylbenzylanilines takes place in the long-wavelength band of the aniline moiety and not in the trichloromethyl or benzyl functionality. Therefore, the methoxy substituent on the aniline ring was changed to methyl and chloro by synthesis of **1c** and **1d**. This replacement results in a blue shift of the long-wavelength band from 3055 Å in **1b** to 2920 Å in **1c** and 2970 Å in **1d** (Table I). It can be seen from this table that the total absorptivity in the solar region has not been dramatically

Table II. Products from Photolysis in Tetrahydrofuran-H₂O

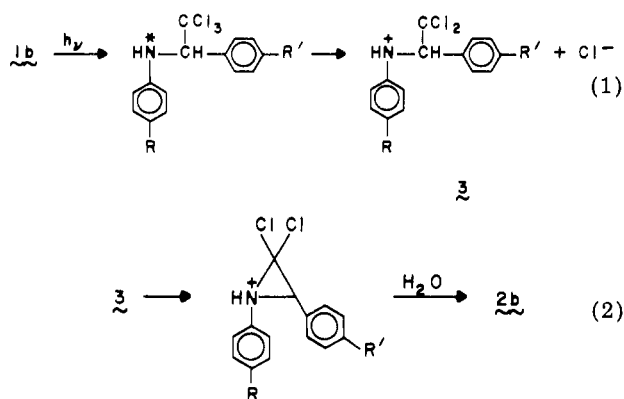
Reactant	R	Products, % yield		
		2	RC ₆ H ₄ -NH ₂	HCOC ₆ H ₄ -OCH ₃
1b	OCH ₃	63	26	16
1c	CH ₃	47	23	13
1d	Cl	57	26	10

affected. A considerable decrease in the rate of photolysis of 1c and 1d compared to that of 1b was, however, measured. Photodecomposition of 1b in tetrahydrofuran-H₂O at 3100 Å is 95% complete in 4 h whereas the conversion of 1c and 1d is incomplete after 3 days under the same conditions. The products from all three compounds were, however, quite similar (Table II).



The reasons for the rate decrease are not entirely clear, but it may be due to the electron withdrawing ability of methyl and chloro compounds compared to methoxy. Thus, stabilization of 1 would result from a smaller relative rate for product formation for an excited intermediate compared to deactivation back to 1.

It has been proposed (Miller et al., 1974) that the initial step after excitation of 1b is electron transfer from the excited aniline to the trichloromethyl group (reaction 1). The rate of this reaction will be governed by the oxidation potential of the aniline and the reduction potential of the trichloromethyl group and should be controllable by varying substituents in the aniline ring. This may account for the very rapid photolysis rate of 1b where the aniline ring is extremely prone to lose an electron. Furthermore, if the hypothesis is correct there, a combination of strongly electron-withdrawing substituents should effectively inhibit the charge-transfer reaction.



To test this hypothesis without synthesizing analogues of 1 photolyses of octyl chloride, decyl bromide, and DDT, sensitized by various anilines, were undertaken. The results are compiled in Table III along with relevant aniline oxidation potentials from cyclic voltammetry ($E_{p/2}$). In each case tetrahydrofuran solutions, exposed to the air, were irradiated at 3100 Å. None of the sensitizers was reactive with octyl chloride which is difficultly reduced.

When *p*-anisidine, *p*-methylaniline, and *N,N*-diethylaniline were used with decyl bromide (easily reduced), a significant decrease in alkyl halide concentration (about 50%) was observed after 36 h. *p*-Chloroaniline or *p*-nitroaniline produced no sensitization. Using DDT (0.05 M) as a substrate with various substituted aniline sensitizers (0.1 M) in tetrahydrofuran, a trend was observed similar to that seen in the case of decyl bromide. It was found that *p*-anisidine, *p*-methylaniline, aniline, *p*-

Table III. Aniline Sensitization of Alkyl Halide Photolysis

ArNH ₂	$E_{p/2(\text{ox})}^a$	Decyl bromide	DDT
<i>p</i> -Methoxyaniline	0.26	+	+
<i>p</i> -Methylaniline	0.40	+	+
<i>N,N</i> -Diethylaniline	0.34	+	N
Aniline	0.54	N	+
<i>p</i> -Chloroaniline	0.60	-	+
2,4-Dichloroaniline	0.78	N	-
<i>p</i> -Nitroaniline	0.97	-	-
2,4-Dinitroaniline	1.48	N	-

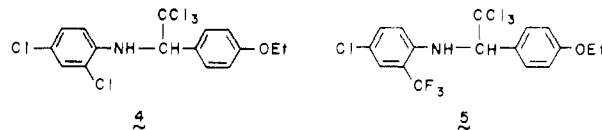
^a $E_{p/2}$ vs. Ag|0.1 M AgNO₃ in CH₃CN. +, sensitization; -, no sensitization; N, not used.

Table IV. Comparison of Insecticide Activities of DDT Analogues

	LD ₅₀ , μg/g		LC ₅₀ , ppm	
	<i>Musca domestica</i>	<i>Phormia regina</i>	<i>Culex fatigans</i> larva	<i>Anopheles albimanus</i> larva
DDT	14.0	11.3	0.07	0.018
Ethoxy-chlor	7.0	6.9	0.04	0.86
1b	15.5	35.2	0.19	0.24
4	12.5		0.053	

chloroaniline, and 4-chloro-2-trifluoromethylaniline sensitized the decomposition of DDT whereas 2,4-dichloroaniline, *p*-nitroaniline, and 2,4-dinitroaniline showed no sensitization.

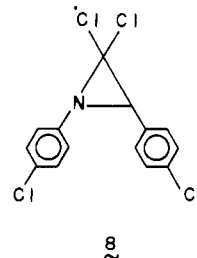
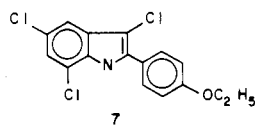
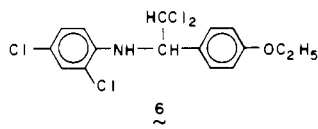
This dependence on oxidation potential of the aniline and reduction potential of the halide is in agreement with the charge-transfer mechanism. Using DDT as a model for the trichloromethyl group of 1 it suggests that a combination of substituents sufficiently electron withdrawing to raise the $E_{p/2}$ of the aniline above ca. 0.7 V should stop electron transfer and stabilize 1. From the above group only 2,4-dichloroaniline possessed functionality considered likely to result in pesticide activity when incorporated into an analogue of 1a. A derivative of 4-chloro-2-trifluoromethylaniline was also of interest since the effects of the trifluoromethyl group would be expected to raise the oxidation potential of the aniline. Hirwe et al. (1972) indicated that the presence of a *p*-ethoxy group in the benzyl ring of 1 in general gave rise to high toxicity. The two compounds synthesized were, therefore, *N*-(α -trichloromethyl-*p*-ethoxybenzyl)-2,4-dichloroaniline (4) and *N*-(α -trichloromethyl-*p*-ethoxy-



benzyl)-4-chloro-2-trifluoromethylaniline (5). When tested for pesticide activity, 5 was found to be inactive while 4 showed activity against the housefly and mosquito larva comparable to that of DDT (Table IV).

Irradiation of 4 was, therefore, performed in the usual manner using tetrahydrofuran-water as solvent. After 70 h only 65% of 4 had reacted. Since this compound has a very similar uv absorbance (Table I) to 1b, it is clear that the excited state reactivity is considerably moderated by the electron-withdrawing substituents. Two major products, 6 and 7, were isolated from this reaction using preparative TLC. 2 was not found.

These results confirm that the reactivity has been greatly changed by making the usual ionic route (reaction 1)



unfavorable. Although a mechanism involving radicals can be formulated to explain 6 and 7, it is considered too speculative for discussion here.

The relative rates of decomposition of 1b, 1c, 1d, 3, and 4 as thin films on glass exposed to sunlight were determined. After irradiating for 4 h in direct winter sunlight, the films were dissolved in tetrahydrofuran and chromatographed by TLC, and the amount of recovered starting compound measured by isolating from the TLC plate and measuring the yield by uv absorption. It was found that 4 and 5 decomposed in a few days, but at a significantly slower rate than the other derivatives.

In field trials of this general class of compounds, trace pesticide activity was found after 2–3 weeks (Metcalf, 1975). These data suggested that the photodecomposition products might possess insecticidal properties. There was no reason to believe that the aldehyde or aniline products would be toxic to insects, but 2 and its analogues do show some similarities in structure to compounds involved in the adrenergic nervous system, i.e. derivatives of mandelic acid. For this reason 2b and 2c were submitted for pesticide screening. The results of these tests showed no activity at 500 $\mu\text{g/g}$ against houseflies or 1 ppm against mosquito larva. Another possibility was that an intermediate dichloroaziridine (Miller et al., 1974) was present in trace amounts and was toxic. Therefore, compound 8 was prepared. However, testing of 8 also showed a complete lack of activity at 500 $\mu\text{g/g}$ against houseflies and

1 ppm against mosquito larva.

SUMMARY

It has been shown that the structure of the photolabile insecticides, 1, can be manipulated to control the lifetime and still retain activity. The success of the mechanistic approach is demonstrated in that a predictable change in reactivity was observed in going from a 4-chloro derivative (1c) to a 2,4-dichloro derivative (4).

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Light-Induced Transformations of Methoxychlor in Aquatic Systems

Richard G. Zepp,* N. Lee Wolfe, John A. Gordon, and Robert C. Fincher

The light-induced decomposition of methoxychlor was studied in hexane, distilled water, and several natural water samples. Product studies indicate that the primary photochemical process for methoxychlor is the same as that for DDT—cleavage of one of its carbon–chlorine bonds to form free-radical intermediates. Subsequent reactions of these intermediates with themselves, oxygen, or the solvent determine the nature of the products. In distilled water, the major product is 1,1-bis(*p*-methoxyphenyl)-2,2-dichloroethylene (DMDE), a DDE analogue. A procedure was developed for computing the direct photolysis rates of pesticides in the aquatic environment. Using this procedure, we estimated that the direct photolysis half-lives of methoxychlor and DDT near the surface of a water body are 4.5 months and greater than 150 years, respectively. Direct photolysis of both DMDE and DDE by sunlight was found to be very rapid. The photolysis rate of methoxychlor under sunlight was found to be much more rapid in several natural water samples (half-lives of 2 to 5 h) than in distilled water. These results indicate that photochemical processes other than direct photolysis cause rapid degradation of methoxychlor in some aquatic environments.

The banning of DDT (except for emergency use) by the U.S. Environmental Protection Agency has spurred the use of several substitutes (Metcalf, 1972). One of the most promising substitutes is methoxychlor, a pesticide that Metcalf (1972) has termed a "persistent yet biodegradable insecticide". The biological degradation has received considerable attention. Although the chemical structure

of methoxychlor is similar to that of DDT, investigations by Kapoor, Metcalf, and their coworkers have indicated that methoxychlor is biodegraded much more rapidly (Kapoor et al., 1970; Metcalf et al., 1971). Biodegradation by higher trophic levels proceeds mainly via O-demethylation, but microbial degradation involves slow dehydrochlorination to bis(*p*-methoxyphenyl)-2,2-dichloroethylene (DMDE), a DDE analogue (Paris et al., 1975).

Only a few previous studies have dealt with the abiotic degradation of methoxychlor. Merna and Eisele (1973)

* Environmental Research Laboratory, U.S. Environmental Protection Agency, Athens, Georgia 30601.