

various authors, and reviewed by Dubois (1961), is needed for the purpose of verifying whether potentiation resulting from the administration of pairs of organophosphorus insecticides to warm-blooded animals was at least in part attributable to impurities of the type under study and present in the products used.

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Photodecomposition of 3',4'-Dichloropropionanilide (Propanil)

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The action of sunlight on dilute aqueous solutions of 3',4'-dichloropropionanilide (propanil) provided a large number of photodecomposition products separable by gas chromatography. 3'-Hydroxy-4'-chloropropionanilide, 3'-chloro-4'-hydroxypropionanilide, 3',4'-dihydroxypropionanilide, 3'-chloropropionanilide, 4'-chloropropionanilide, propionanilide, 3,4-dichloroaniline, 3-chloroaniline, propionic acid, propionamide, 3,3',4,4'-tetrachloroazobenzene, and a humic acid were identified. The

tetrachloroazobenzene also resulted from the photolysis of a dilute aqueous solution of 3,4-dichloroaniline. The principal pathways of propanil photodecomposition were: replacement of chlorine substituents by hydroxyl groups; formation of propionamide; replacement of chlorine substituents by hydrogen; and hydrolysis of the amide. Propanil and its benzenoid photolysis products were not appreciably volatile, and only propanil was phytotoxic.

The anilide herbicide 3',4'-dichloropropionanilide (propanil, I) is widely used for the selective control of broad-leaf weeds in cultivated rice and as a postemergence herbicide in tomatoes. In 1968, a controversy developed over the use of propanil in the vicinity of prune orchards in several Northern California counties after some of the trees began to exhibit yellowing of the leaves allegedly due to incidental exposure to the herbicide following its use in nearby rice fields.

The purpose of the present investigation was to identify the products of propanil photodecomposition in aqueous solution, to propose a possible mechanism for their formation, and to determine whether or not the photodecomposition of propanil was related to prune tree damage.

EXPERIMENTAL

Synthesis of Photoproducts. 3',4'-Dichloropropionanilide was received as a technical product, mp 85–89°C (Technical Stam, Rohm & Haas Co.). It was recrystallized twice from

cyclohexane (charcoal) to a mp of 91–92°C [lit. 91–92°C (Good, 1961)].

3'-CHLOROPROPIONANILIDE (II). Propionyl chloride (0.92 g, 0.010 mol) was slowly added to a chilled suspension of 3-chloroaniline (Eastman Organic Chemicals) (1.28 g, 0.010 mol) in 6 ml of 10% sodium hydroxide solution to give 3'-chloropropionanilide (0.92 g, 50%) which was recrystallized twice from 3:1 water-ethanol; mp 85.5–86°C [lit. 88–89°C (Good, 1961)].

Anal. Calcd for $C_9H_{10}ClNO$: C, 58.85; H, 5.49; N, 7.65. Found: C, 59.00; H, 5.30; N, 7.70.

Infrared (ir) spectrum 3236 (NH) and 1667 (CO) cm^{-1} . Nuclear magnetic resonance (nmr) spectrum δ 8.80 (NH). Mass spectrum m/e 183 (parent), 127 (base, $ClPhNH_2$).

4'-CHLOROPROPIONANILIDE (III). The procedure was identical to that for 3'-chloropropionanilide except that 4-chloroaniline (Eastman Organic Chemicals) was used to give 4'-chloropropionanilide (0.84 g, 46%) which was recrystallized twice from benzene; mp 137.5–139°C [lit. 137°C (Good, 1961)].

Anal. Calcd for $C_9H_{10}ClNO$: C, 58.85; H, 5.49; N, 7.65. Found: C, 58.96; H, 5.39; N, 7.44.

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Ir spectrum 3333 (NH) and 1675 (CO) cm^{-1} . Nmr spectrum δ 9.20 (NH). Mass spectrum m/e 183 (parent), 127 (base, $\text{C}_6\text{H}_5\text{NH}_2$).

3'-CHLORO-4'-HYDROXYPROPIONANILIDE (V). 2-Chloro-4-nitrophenol (Aldrich Chemical Co.) (10.0 g, 0.058 mol) in absolute ethanol (200 ml) was reduced to the corresponding amine with platinum oxide (Adams Catalyst) and hydrogen at ambient temperature and pressure. The resulting 2-chloro-4-aminophenol was propionylated at the amino group by dissolving it in propionic acid (120 ml) and adding a slight excess of propionic anhydride (7.2 ml). After heating on a steam bath for 1.5 hr, the mixture was poured over ice to give 3'-chloro-4'-hydroxypropionanilide (2.7 g, 23.5%) which was recrystallized twice from water; mp 140–141.5°C.

Anal. Calcd for $\text{C}_9\text{H}_9\text{ClNO}_2$: C, 54.26; H, 5.06; N, 7.03. Found: C, 54.14; H, 4.98; N, 7.04.

Ir spectrum 3413 (NH), 3205 (PhOH), and 1667 (CO) cm^{-1} . Nmr spectrum δ 8.68 (PhOH) and δ 9.17 (NH). Mass spectrum m/e 199 (parent), 143 (base, $\text{C}_6\text{H}_5\text{NH}_2\text{OH}$).

3'-HYDROXY-4'-CHLOROPROPIONANILIDE (VI). A solution of 2-amino-5-nitrophenol (Eastman Organic Chemicals) (61.6 g, 0.400 mol) in concentrated hydrochloric acid (260 ml) was diazotized with sodium nitrite (28.8 g, 0.400 mol) in water (70 ml), and the diazonium salt was treated with cuprous chloride (40 g, 0.400 mol) in water (200 ml) to give 2-chloro-5-nitrophenol (3.4 g, 4.9%). This compound was catalytically hydrogenated, followed by propionylation at the amino group as described above to give 3'-hydroxy-4'-chloropropionanilide (1.5 g, 31%) which was crystallized twice from 4:1 water-ethanol; mp 206–207°C.

Anal. Calcd for $\text{C}_9\text{H}_9\text{ClNO}_2$: C, 54.26; H, 5.06; N, 7.03. Found: C, 54.19; H, 4.99; N, 7.06.

Ir spectrum 3344 (NH), 1661 (CO) cm^{-1} . Nmr spectrum δ 8.72 (PhOH) and δ 9.17 (NH). Mass spectrum m/e 199 (parent), 143 (base, $\text{C}_6\text{H}_5\text{NH}_2\text{OH}$).

3',4'-DIHYDROXYPROPIONANILIDE (VIII). 4-Nitrocatechol (Aldrich Chemical Co.) (5.0 g, 0.032 mol) in absolute ethanol (100 ml) was catalytically hydrogenated and then propionylated at the amino group as described for the previous two compounds to give 3',4'-dihydroxypropionanilide (4.7 g, 81%) which was recrystallized twice from water; mp 200°C (dec).

Anal. Calcd for $\text{C}_9\text{H}_{11}\text{NO}_3$: C, 59.64; H, 6.12; N, 7.73. Found: C, 59.45; H, 6.24; N, 7.58.

Ir spectrum 3390 (PhOH), 3344 (NH), and 1587 (CO) cm^{-1} . Nmr spectrum δ 8.72 (PhOH) and δ 9.48 (NH). Mass spectrum m/e 181 (parent), 125 (base, $\text{PhNH}_2(\text{OH})_2$).

3,3',4,4'-Tetrachloroazobenzene (XIV) was prepared by the method of Corbett and Holt (1963) and recrystallized twice from benzene-petroleum ether; mp 158–158.5°C. Standard humic acid (XII) was prepared by the method of Crosby and Tutass (1966).

Methods. All melting points were determined on a Hoover capillary melting point apparatus and are uncorrected. Ir spectra were measured in KBr micropellets with a Perkin-Elmer Model 337 grating spectrophotometer. Ultraviolet spectra were measured in aqueous solution on a Beckman DK-2A spectrophotometer. Nmr spectra were measured with a Perkin-Elmer Hitachi Model R-20 spectrometer as solutions in deuterated acetone or deuterated dimethyl-sulfoxide with a tetramethylsilane internal standard. Mass spectra were recorded with a Varian M-66 instrument. Elemental analyses were performed by the Microanalytical Laboratory of the Chemistry Department at the University of California, Berkeley, Calif.

Gas-liquid chromatographic (glc) analyses were accomplished with an F&M Model 720 instrument equipped with a thermal conductivity detector and 2-ft \times $\frac{1}{8}$ -in. i.d. stainless steel columns containing either 2% SE-30 silicone gum on 60/80 mesh acid-washed, DMCS-treated Chromosorb G, or 1% diethylene glycol adipate (DEGA) on 100/120 mesh acid-washed, DMCS-treated Chromosorb G (Perco Supplies, San Gabriel, Calif.). The initial column temperature was 50°C; final column temperature, 200°C (DEGA) or 280°C (SE-30); program rate, 10°C per min; injection port temperature, 250°C; detector temperature, 300°C; helium carrier gas, flow rate 40 ml per min. As it eluted, each compound was collected in a glass capillary tube, purified by rechromatography, and identified by comparison of its spectra, mp, and chemical properties with those of authentic specimens.

Thin-layer chromatography (tlc) was carried out on Brinkmann Silica Gel F-254 (0.5-mm thickness) containing 1% zinc orthosilicate:manganese phosphor using benzene-ethyl acetate-methylene chloride (9:7:3, v/v/v). Detection of phenolic compounds employed 1% *p*-nitrobenzenediazonium fluoborate in 20% aqueous sodium acetate. The R_f values for several of the photoproducts are: Compound II, 0.51; III, 0.49; V, 0.35; VI, 0.32; VII, 0.14; XIV, 0.77.

Standard solutions for irradiation were prepared by dissolving 200 mg of propanil in 1 l. of distilled water. A preparative-scale photoreactor which closely simulated the effects of sunlight was employed for laboratory irradiations (Crosby and Li, 1969; Crosby and Tang, 1969); samples for isolation and identification usually were prepared in this equipment.

Irradiations with sunlight were conducted with 200-ppm solutions prepared by dissolving 3.4 g of propanil in 17 l. of distilled water in a covered, 40-l. borosilicate glass bottle. To ensure aerobic conditions and agitation, filtered compressed air was bubbled in through a glass frit. The solution was allowed to remain outdoors for 6 months, and aliquots were analyzed at frequent intervals.

The irradiated solutions were adjusted to pH 11 with aqueous sodium hydroxide solution, extracted with three portions of ethyl ether, and the combined extracts were washed with a small amount of water, dried (MgSO_4), and evaporated to a small volume on a rotary evaporator. Each aqueous phase was acidified to pH 2 with a few drops of dilute hydrochloric acid and extracted in the same way. The volume of each concentrated extract was reduced further to about 0.5 ml in a centrifuge tube under a stream of nitrogen.

Toxicity Measurements. The phytotoxicity of irradiated propanil solutions was determined with 6-month-old prune trees (*Prunus domestica* L., var. French) grown outdoors in 5-gal cans. A 200-ppm propanil solution was stored in the dark as a control (Solution I), while an identical solution was exposed to sunlight for 3 days (Solution II) for formation of early photolysis products. (Some photolysis had occurred during the 3-day period, since the pH of the solution dropped from 7 to about 5.5, and a glc profile showed very small amounts of several of the characteristic peaks.) Another solution was exposed to sunlight for 1 month (Solution III) to obtain steady-state photolysis products.

To differentiate between volatile and nonvolatile photoproducts, 1 l. of a 200-ppm aqueous propanil solution, exposed to sunlight for 1 month, was evaporated to dryness in an all-glass rotary evaporator. The solid residue of non-volatile products was redissolved in 1 l. of water (Solution V), while the condensate provided Solution IV.

The test solutions, containing 0.1% Triton 100 wetting

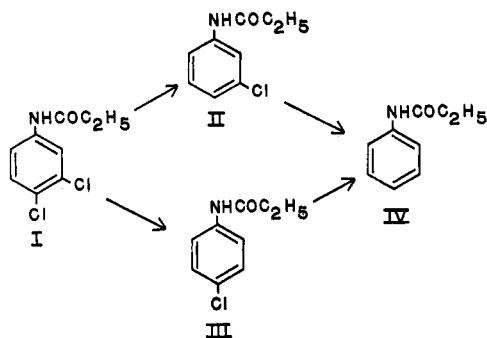


Figure 1. Photoreduction of propanil

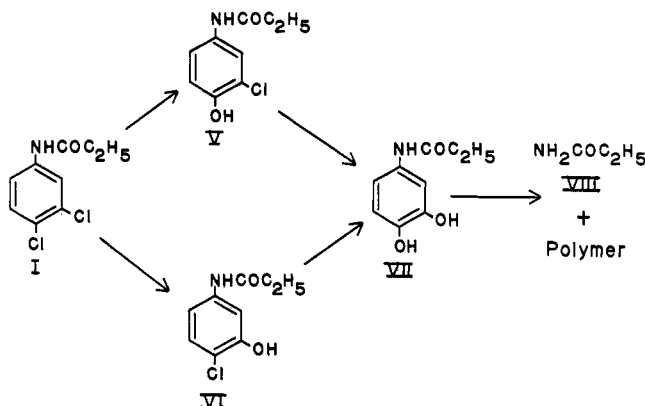


Figure 2. Formation of hydroxylated analogs of propanil

agent, were applied to each surface of the leaves with a cotton swab. Leaves of a separate tree received Triton 100 solution (Solution VI) as a control. After 5 weeks, the number of missing and damaged (yellow) leaves was recorded.

Volatility Measurements. To determine whether propanil itself codistilled with water, a 50-ppm solution contained in a 2-l. flask was immersed in a constant temperature bath at 35°C. The concentration of propanil was determined each day by measuring its ultraviolet spectrum.

To check for the possibility of volatile photolysis products, a stream of air was bubbled through the reactor and into a trap as photolysis took place. The trap consisted of several hundred milliliters of isopropyl alcohol immersed in a Dry Ice-propylene glycol cold bath. In each experiment the photolysis was conducted for 1 week, after which the isopropyl alcohol solution was evaporated to a small volume and analyzed for products by thin-layer and gas chromatography.

RESULTS AND DISCUSSION

Both in sunlight and in the laboratory, propanil solutions gradually became yellow and, eventually, dark brown. However, decomposition of the herbicide was slow, and 18% still remained unchanged after irradiation of a 200-ppm solution in the photoreactor for 34 days.

Comparison of the glc profiles of extractives from both outdoor and laboratory photolyses demonstrated the close simulation of sunlight conditions by the more controllable reactor. The profiles were unusually complex and changed rapidly as irradiation progressed. However, the accumulation of several major conversion products was evident; 3'-chloropropionanilide (II), 3-chloroaniline (XV), 3,4-dichloroaniline (XIII), and the rather volatile propionamide (VIII)

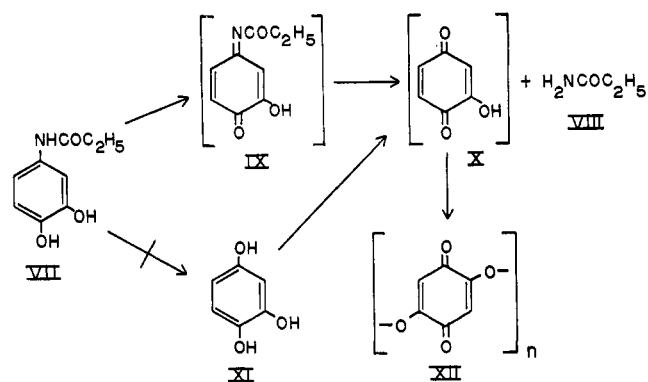


Figure 3. Proposed photooxidation of propanil. Compounds IX and X are hypothetical

were identified. Prolonged irradiation led to dark, unextractable materials.

The reductive formation of II was to be expected; similar examples of the replacement of ring halogens by hydrogen are well-known (Crosby and Li, 1969; Plimmer, 1970). Predictably (Plimmer, 1970), the 3-chloro isomer should be more stable than the 4'-chloropropionanilide (III) to further photolysis; examinations of the small glc fraction having the same retention time as authentic III confirmed that both isomers indeed were formed during photolysis. Further irradiation of 100-ppm solutions of either II or III produced unsubstituted propionanilide (IV) (Figure 1). Obviously, II is more stable than I toward light and is the principal photolysis product to accumulate, but it exhibits only 5.8% of the herbicidal activity of I (Good, 1961).

Previous experience also has shown the replacement of ring chlorines by hydroxyl to be a general reaction (Crosby and Li, 1969; Plimmer, 1970). The acidity of the propanil solution gradually increased from pH 7.5 to pH 2.8 as photolysis proceeded, and the precipitation of silver chloride upon addition of silver nitrate solution confirmed the dechlorination. Several phenolic products showing a yellow color with *p*-nitrobenzenediazonium fluoroborate were detected on thin-layer chromatograms, but concentrations amounted to only 0.1 ppm. Using authentic 3'-chloro-4'-hydroxypropionanilide (V), 4'-chloro-3'-hydroxypropionanilide (VI), and 3',4'-dihydroxypropionanilide (VII) for reference, these three possible dechlorinated products were isolated from the photolysis mixture and identified spectrometrically.

Irradiation of 100-ppm solutions of V and VI also produced detectable VII, but all three compounds were converted rapidly into VIII and dark insoluble matter, suggestive of their oxidation to quinones (Figure 2). VIII was detectable after 5 days of irradiation in the reactor, and its stability resulted in an eventual yield of 14% after 46% of the propanil had been photolyzed. The oxidation of other acylamino-phenols with lead tetraacetate or chromium trioxide under very mild conditions results in the formation of the corresponding *p*-benzoquinone *N*-acylimides (Adams and Looker, 1951) which are spontaneously hydrolyzed in the presence of water to yield the quinone and amide. Consequently, as proposed in Figure 3, VII could undergo photooxidation to the transient quinone imide (IX) which would produce 2-hydroxy-*p*-benzoquinone (X) and VIII in the aqueous medium; X would be converted to a polymeric humic acid XII (Bremner, 1967; Crosby and Tutass, 1966; Ziehmman and Scholy, 1960) under the reaction conditions. In view of the well-known inhibition of photosynthesis by quinones (Zweig, 1969), it appears that the herbicidal activity of acyl-

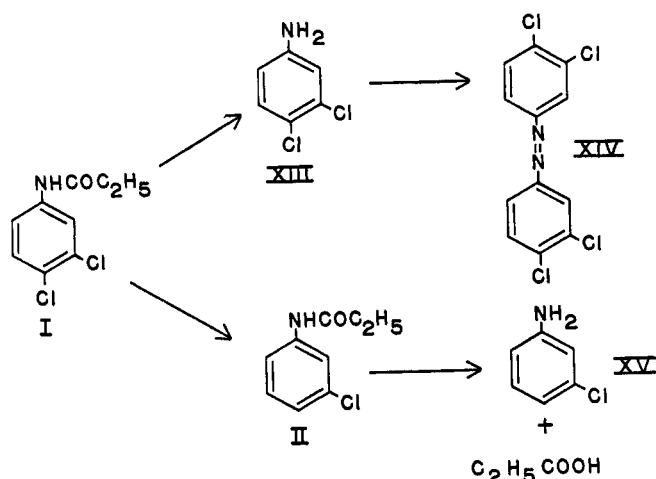


Figure 4. Formation and fate of chloroanilines

anilides such as propanil may lie in their ability to undergo metabolic conversion to chloroquinones within the plant.

The dark insoluble substance isolated from the photolysis mixtures indeed exhibited an ir spectrum identical to that of synthetic humic acid prepared from 1,2,4-benzenetriol (XI), but attempts to detect XI itself (Crosby and Tutass, 1966) were consistently unsuccessful. Efforts to isolate IX are continuing.

Photolytic formation of anilines from corresponding amides and ureas has been reported (Crosby and Tang, 1969; Elad *et al.*, 1965), so the appearance of XIII and XV as major transformation products of propanil was not surprising (Figure 4). However, the irradiation of a 100-ppm solution of XIII resulted in rapid photodecomposition and isolation of 3,3',4,4'-tetrachloroazobenzene ("TCAB"), presumably through the intermediate formation of 3,4-dichloronitrosobenzene. TCAB has been reported as a metabolite of propanil formed by soil microorganisms (Bartha and Pramer, 1967; Chisaka and Kearney, 1970), and also by the irradiation of XIII in the presence of sensitizers (Plimmer and Kearney, 1969; Rosen *et al.*, 1969).

Due to the fact that all of the photodecomposition products, except II, break down at a much faster rate than propanil, no mechanistic studies or quantitative data were obtained for the three pathways contributing to the total photolysis. Qualitatively, each of the pathways contributes significantly to the overall breakdown, since the concentrations of photolysis products arising from each correspond within one order of magnitude after steady state conditions are achieved.

The propanil solution held in the dark (Solution I) caused a high degree of phytotoxicity (Table I), and short-term irradiation caused little change (Solution II). However, a month's exposure to sunlight (Solution III) resulted in distinct reduction in effects, with all activity concentrated in the non-volatile fraction (Solution V) rather than in the distillate (Solution IV).

The volatility measurements (Table II) revealed that the concentration of propanil increased as water evaporated. After 1 week, there was no detectable loss of propanil from the solution, indicating that it does not codistil with water.

Table I. Phytotoxicity of Propanil and Its Photoproducts

Solution no.	Leaves dropped, %	Remaining leaves, damaged, %	Total leaves affected, %
I (control)	53	17	70
II	51	13	64
III	37	9	46
IV	0	0	0
V	32	12	44
VI (control)	0	0	0

Table II. Attempted Volatilization of Propanil^a

Time, days	Volume, ml	Propanil conc, mg/l.	Remaining propanil, mg
0	2000	50.0	100.00
1	1925	52.0	100.10
2	1838	54.5	100.17
3	1740	57.5	100.05
4	1620	61.7	99.95
5	1480	67.5	99.90
6	1283	78.0	100.07

^a Initial amount was 100 mg.

No volatile aromatic photoproducts of propanil were ever detected.

The results show that the observed phytotoxicity in orchards can be attributed to propanil itself, probably in particulate form. Sunlight may act to reduce the effect through the photodecomposition of the herbicide, as the photolysis products are nontoxic to young prune trees.

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