Photolysis of Pesticidal Synergists.
I. Piperonyl Butoxide

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The discovery and subsequent development of pesticidal synergists represents an important advance in pest control in that it primarily affords the prospect of reducing the amounts of insecticides in man's environment. Foremost in importance are the methylenedioxyphenyl synergists, e.g., piperonyl butoxide, sesamex, sulfoxide, bucarpolate, sesamolin, sesamin, tropital, n-propyl isome and piperonyl cyclonene. The synergistic action of these compounds is generally attributed to enzyme inhibition or prevention of induction of the mixed function oxidases, hence interference with detoxification thus leading to retention and accumulation of the toxic insecticide or its derivative.

Recent attention has focused on the *potential* hazards to man from piperonyl butoxide (and related synergists) due to their enhancement of acute toxicity of agents such as benzo(a)pyrene, griseofulvin (1) and certain fluorocarbons such as Freons (2) as well as their comparative slow rate of elimination and evidence of unmetabolized residues in the lung following various routes of administration to the rat (3-5).

Since human exposure to synergists (primarily piperonyl butoxide) is *via* inhalation of aerosols in addition to ingestion from the use of sprays, wettable powders and impregnated kraft linings containing this agent, it is of paramount importance to elicit the stability of these agents to light and temperature under a variety of conditions.

Materials and Methods

Both piperonyl butoxide, technical grade (87%) (Aldrich Chemical Co.) and redistilled synergist, b.p. 180^{o}/1 mm, were exposed under the following photolytic conditions: (a) irradiation for periods of 7 days in open Pyrex crystallizing dishes in an environmental "weathering chamber" (6), with a General Electric

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sunlamp (275W, peak absorbance 2967Å) at a distance of 22.54 cm. The photochemical activating light level intensity at this distance was 8.5 x 10^6 ergs/cm^2/sec. (850 MW/cm^2) recorded with a Kettering "YSI Model 65" radiometer with a fused quartz window probe (250-3,300 mμ) (Yellow Springs Instrument Co.). The temperature of exposure was 53°C.; (b) irradiation in 500 ml water-cooled, photochemical borosilicate and quartz immersion wells using an Hanovia 450W mercury lamp with and without filters; (c) irradiation in Pyrex crystallizing dishes in outdoor sunlight.

Unirradiated controls were examined in analogous determinations and both TLC and GLC were utilized for the separation and detection of photochemical products following concentration of the samples under vacuo. TLC utilized (a) silica gel GF with chloroform-acetic acid-water (2:1:1) and n-butanol-acetic acid-water (6:1:2) as developers and 1% aqueous ferric chloride-potassium ferricyanide and 1% aqueous p-phenylenediamine as detecting reagents; (b) silica gel G with 2.5% acetone in benzene and butanol-water (90:10) as developing solvents and chromotropic-sulfuric acid spray (7), silver nitrate-2-phenoxy ethanol (8) and benzidine-periodate (9) as chromogenic reagents. Gas-liquid chromatographic analyses were performed on an F&M 700-1099F Laboratory Chromatograph equipped with a Hewlett-Packard Model 240 temperature programmer, flame ionization detector, and 6 ft. x 1/8 in. stainless steel columns loaded with (a) 4% QF-1 on 80/100 mesh HMDS Chromosorb W; (b) 3% Carbowax 20 M on 80/100 mesh HMDS Chromosorb W.

Results and Discussion

The relative stability of piperonyl butoxide under a variety of extreme conditions of irradiation was evidenced by the following observations: (a) Irradiation in a "weathering chamber": whereas the irradiation of piperonal (10) for periods as brief as 3 hours resulted in the formation of protocatechualdehyde, protocatechuic acid and tetrahydroxy-p-benzoquinone (11) *via* opening of the methylenedioxy ring, as well as piperonylic acid and polymer, the exposure of both technical and purified piperonyl butoxide for periods of 7 days followed by extraction with methanol and concentration under vacuum yielded primarily unphotolyzed synergist (95% by weight) (retention times 25.3 and 23.7 mins., respectively, on 3% Carbowax and 4% QF-1 columns at 275°C) and black polymer of unresolved structure. No evidence of a catecholic type degradation could be discerned by chromogenic agents specific for phenolic moieties, e.g., aqueous ferric chloride-potassium ferricyanide and p-phenylenediamine following two-dimensional TLC on silica gel GF with chloroform-acetic acid-water (2:1:1) and n-butanol-acetic acid-water (6:1:2) as developers or *via* silylation of the reaction mixture and gas-liquid chromatography. (b) Irradiation with a 450W Hanovia mercury lamp: 96-98% by weight of unreacted piperonyl butoxide was recovered

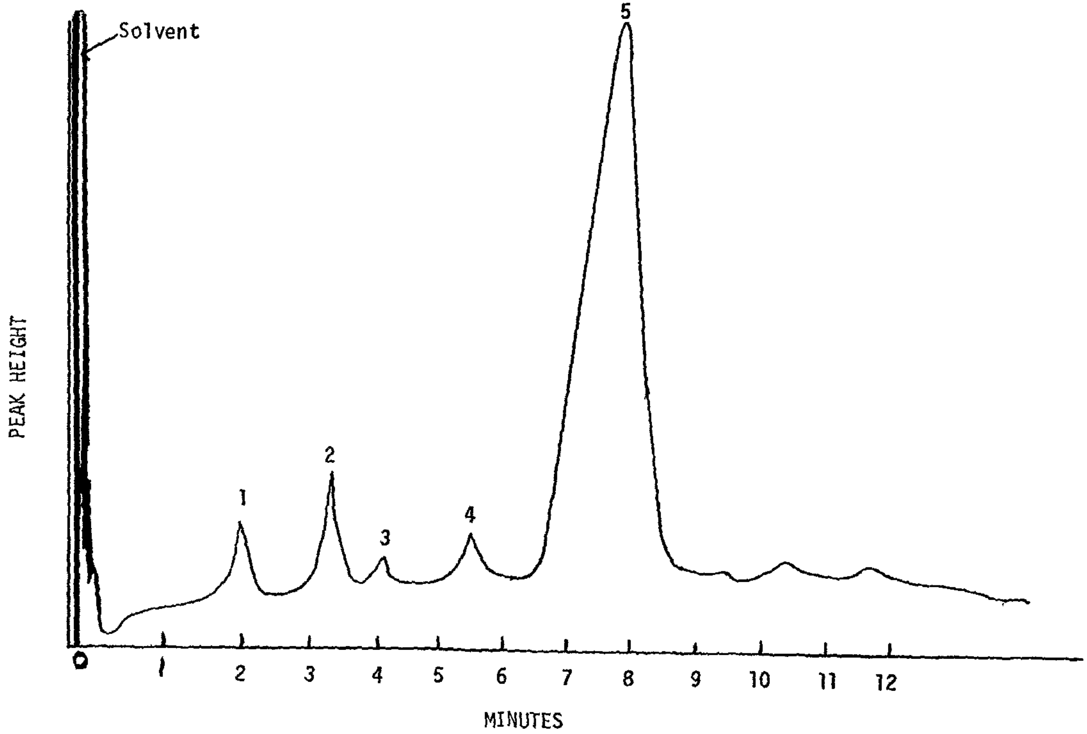

Fig. 1. Programmed temperature gas chromatographic separation of piperonyl butoxide photodegradation products on 4% QF-1 coated HMDS Chromosorb W 80/100, 6'x1/8" i.d., injection port and detector 240 and 260°C, respectively. Oven programmed linearly 15°/min. from 110° to 240°C. Carrier gas: helium 40 ml/min. 1=ethylene glycol; 2=butyl carbitol; 3=unknown; 4=propyl-3,4-methylenedioxy-toluene and 5=piperonyl butoxide.

(following concentration under vacuum, same GLC retention times as above) when commercial and purified piperonyl butoxide, respectively, were irradiated in absolute methanol in a borosilicate photochemical immersion well for 89 hours with a 450W Hanovia mercury lamp equipped with a vycor filter (cut-off 210 mμ, 50% transmission at 240 mμ). Irradiation of safrole (1-allyl-3,4-methylenedioxybenzene, an intermediate in the manufacture of piperonyl butoxide) under analogous conditions and work-up yielded 1-cyclopropyl-3,4-methylenedioxybenzene in over 90% yield by weight _via_ a suggested internal sensitized photocyclization process (12). (c) Irradiation with 450W Hanovia mercury lamp (unfiltered): Irradiation for up to 5 weeks of 10% solutions of samples of piperonyl butoxide in cyclohexane or benzene in a borosilicate photochemical immersion well using a 450W Hanovia mercury lamp (unfiltered lamp, light from 190 nM and greater) did not result in any measurable degradation as ascertained by TLC and GLC procedures described above. However, the irradiation (Hanovia 450W lamp, no filters) of a 10% solution of purified piperonyl butoxide in benzene in a quartz immersion well for 18 days resulted in the formation of a small amount (approximately 2-3% by weight) of butyl carbitol as well as ethylene glycol and propyl-3,4-methylenedioxy-toluene (separated and identified by TLC, GLC, NMR and I.R.).

Methanolic extracts of the above irradiation were separated by two-dimensional TLC on silica gel-G _via_ initial development with 2.5% acetone in benzene (unreacted piperonyl butoxide and propyl-3,4-methylenedioxy-toluene, R_F 0.32 and 0.20, respectively, were detected with the chromotropic-sulfuric acid spray), followed by 90° development with butanol-water (90:10) for the separation of ethylene glycol and butyl carbitol (R_F .42 and 0.27 detected with the benzidine-periodate and silver nitrate reagents, respectively).

Figure 1 is a chromatogram illustrating the separation of the products of the above irradiation (e.g., butyl carbitol, ethylene glycol, propyl-3,4-methylenedioxy-toluene, piperonyl butoxide and unknown) obtained by treating the reaction mixture with hexamethyl disilazane-trimethyl chlorosilane (2:1) with pyridine as solvent (13). The programmed temperature gas chromatographic separation was accomplished using a 6 ft. x 1/8 in. stainless steel column of 4% QF-1 on 80/100 mesh HMDS Chromosorb W, temperatures of injection port and detector were 240 and 260°C, respectively; column initially at 110°C then programmed at the rate of 15°/min. to 240°. Flow rates of helium, hydrogen and air were 40, 21 and 300 ml/min., respectively. Figure 2 illustrates the photodecomposition of piperonyl butoxide in benzene when irradiated in a quartz reactor with a 450W Hanovia mercury lamp (unfiltered).

Individual constituents resolved by GLC were isolated _via_ the insertion of a Pasteur pipet through a Neoprene septum into the exit port of the chromatograph and their infrared and N.M.R. spectra measured with a Perkin-Elmer 621 Infrared Spectrophotometer

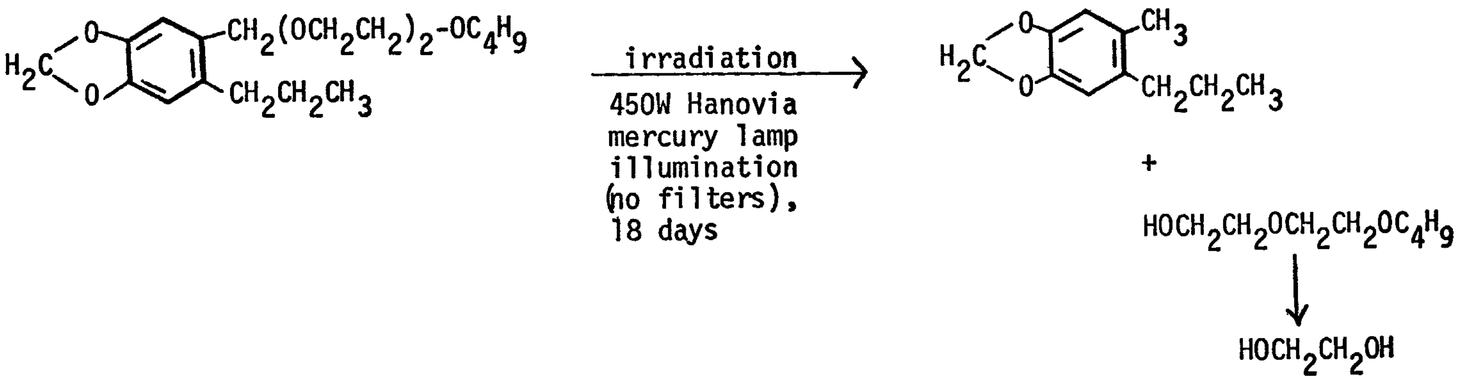

Fig. 2. Photodecomposition of piperonyl butoxide.

and Varian HA-100 Nuclear Magnetic Spectrometer and were identical with those of known constituents collected under analogous gas chromatographic conditions.

(d) Irradiation in outdoor sunlight: Both commercial and purified piperonyl butoxide were exposed in Pyrex crystallizing dishes covered with a layer of perforated Saran wrap to outdoor sunlight for periods of up to one week. Following methanolic extraction and concentration under vacuum the samples were examined by TLC, GLC and NMR. A dark brown product, presumably polymeric, was isolated in yields of 3 and 1.5% by weight, respectively, (as well as 96% and 98% piperonyl butoxide by weight), from commercial and purified piperonyl butoxide samples following 7 days' exposure. There were no appreciable losses due to volatility. However, TLC analysis of the methanolic concentrate of the irradiated commercial sample utilizing silica gel G with 2.5% acetone in benzene as developer and chromotropic-sulphuric spray indicated two minor components of unknown structure at R_F 0.40 and 0.50, respectively. (The infrared spectrum of both had bands at 950 cm^{-1} (methylenedioxy), and the presence of the methylenedioxy group was also indicated by a positive Labat test.) The GLC retention times of the above unknown irradiated products were 20 and 22 minutes, respectively, on 3% Carbowax at 275°C and their combined recoveries based on GLC being 0.5% by weight. These products were not found in any of the other photolytic experiments described above.

Friedman and Epstein (14) have recently noted the photochemical and thermal stability of thin films and vials of 70% commercial piperonyl butoxide to both fluorescent illumination and heating to 100°C for 7 and 5 days, respectively.

Our studies illustrate the relative stability of piperonyl butoxide under a variety of photolytic conditions. Further studies would appear to be relevant to ascertain conditions under which this apparent stability of piperonyl butoxide coupled with its micorosmal enzyme inhibition, enhancement of drug toxicity and comparative slow mammalian elimination could constitute an incipient environmental hazard.

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