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Investigation of the Mechanism and Pathway of Biphenyl Formation in the Photolysis of Monuron

Fred S. Tanaka,* Ronald G. Wien, and Barry L. Hoffer

In the photolysis of 3-(4-chlorophenyl)-1,1-dimethylurea (monuron), where labile hydrogen was readily available, photodechlorination was a major reaction leading to the production of 3-phenyl-1,1-dimethylurea (fenuron) and the 2,4'-, 3,4'-, and 4,4'-bis(*N',N'*-dimethylureido)biphenyls (fenuron biphenyls). Three pathways appeared to be available for fenuron biphenyl formation; however, yields of isomeric fenuron biphenyls under different reaction conditions revealed that photoexcited monuron coupled with fenuron at only the ortho and para positions. The meta-coupled biphenyl was obtained by first forming a chlorinated biphenyl, which was subsequently dechlorinated to yield product. Coupling of two fenuron molecules did not occur. Inhibition studies of photocoupling indicated that biphenyls were being formed via a neutral free radical. An addition–elimination mechanism is suggested as a process that would account for the identified products and for the observed regioselectivity.

In the photolysis of aqueous solutions of monuron, photocoupled products were detected and isolated. After partial characterization, these products appeared to be substituted diphenylamines (Tanaka et al., 1977). After further investigation, however, the coupled photoproducts were clearly identified as isomeric biphenyl compounds (Tanaka et al., 1981). In the presence of nonionic surfactants, photolyzed monuron afforded photodechlorinated biphenyls as well as the monochlorinated biphenyls (Tanaka et al., 1979). Therefore, a study was undertaken to identify the isomeric fenuron biphenyls, to determine their pathways of formation, and to obtain information concerning the mechanism of their formation in monuron photolysis.

EXPERIMENTAL SECTION

Materials and Equipment. Triton X-100 and Tergitol TMN-10 were purchased from Sigma Chemical Co. 2- and 4-phenylpyridines were obtained from Aldrich Chemical Co. 3-Phenylpyridine was prepared by a procedure that gave a mixture of three isomeric phenylpyridines (Bachmann and Hoffman, 1944). The 3-phenylpyridine (R_f = 0.4) was separated from the isomeric mixture by preparative thin-layer chromatography (TLC) using 0.5 mm thick silica gel HF plates with a developing solvent of toluene–acetone (10:1 v/v).

[*methyl*-^{14}C]Fenuron was prepared from 0.1 mCi of [^{14}C]dimethylamine hydrochloride (9.64 mCi/mmol) purchased from New England Nuclear Corp. by using a previously developed microscale procedure (Tanaka, 1970). Radiolabeled fenuron was purified by high-performance liquid chromatography (HPLC) and then diluted with carrier material to a specific activity of 0.9 mCi/mmol.

The methods of purification, identification, and quantitation were basically the same as those described earlier (Tanaka et al., 1977, 1979, 1981). Photoreactions were conducted with a Rayonet RPR-204 reactor (The Southern New England Ultraviolet Co.) equipped with four sunlight RUL-3000 lamps (21 W) with peak spectral energy distribution at 300 nm. The mass spectrometer, nuclear magnetic resonance (NMR) spectrometer, liquid scintillation counter (LSC), HPLC, and other equipment employed for this study were the same as those listed earlier (Tanaka et al., 1981). TLC was performed on 0.25 mm thick plates of Anasil HF (Analabs), and the developing solvent was benzene–acetone (2:1 v/v) unless specified otherwise. HPLC was performed with 10-μm Radial-Pak (Waters Associates) columns of either CN or C_{18} with an isocratic elution solvent of 18% acetonitrile in water unless specified otherwise.

Identication of the Isomeric Fenuron Biphenyls. Three 500-mL samples were prepared; each contained 75 ppm of fenuron (10 μCi of [*methyl*-^{14}C]fenuron) and 75 ppm of monuron. To one sample was added Tergitol TMN-10 and to a second sample was added Triton X-100 to prepare aqueous surfactant solutions of 0.2% (w/v). All samples were degassed with nitrogen, temperature equilibrated (52 °C), and irradiated for 135 min. The fenuron biphenyls were isolated by preparative TLC, and the correct band was located by using a reference standard (R_f

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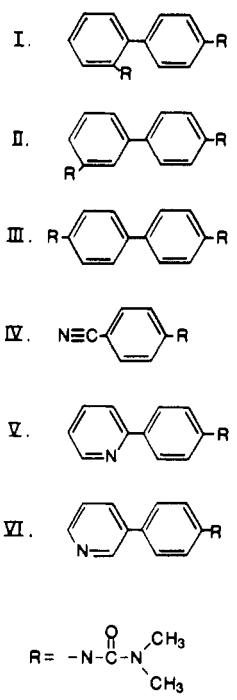


Figure 1. Structures of synthesized standards.

Table I. Liquid Chromatographic Separation of Dechlorinated Isomeric Biphenyls from Monuron Photolysis

compound[b]	retention time, min[a] Radial-Pak C_{18}	Radial-Pak CN
2,4′ isomer	12.2	6.9
3,4′ isomer	17.1	11.2
4,4′ isomer	14.6	11.2

[a] Isocratic solvent was 18% acetonitrile in water, and the flow rate was 3 mL/min. [b] Isomers of bis(*N′,N′*-dimethylureido)biphenyls (I, II, and III).

= 0.2). The biphenyls were eluted from silica gel and further purified by HPLC using a Radial-Pak CN column. A major peak and a minor peak were observed by HPLC. The materials from the two peaks were trapped and further purified by HPLC with a Radial-Pak C_{18} column whereby the minor peak was resolved into two components. The mass spectra of the three isolated biphenyls all showed molecular ions of *m/e* 326 corresponding to dechlorinated substituted biphenyls (Figure 1, structures I, II, and III).

2,4′-Bis(*N′,N′*-dimethylureido)biphenyl (I). Approximately 100 mg (0.31 mmol) of 5-chloro-2,4′-bis(*N′,N′*-dimethylureido)biphenyl prepared earlier (Tanaka et al., 1981) was added to 1 mL of piperidine and diluted to 100 mL with distilled water. The material in solution was photolyzed for 150 min in the Rayonet reactor to effect reductive dechlorination. The product was extracted with ethyl acetate, concentrated, and purified by TLC (R_f = 0.2) followed by HPLC using a Radial-Pak CN cartridge (Table I): mass spectrum *m/e* (rel intensity) 326 (M^+, 52), 281 (99), 236 (43), 72 (100), 46 (52), 44 (56); ^1H NMR (Me_2SO-d_6) δ 2.78 (s, 6 H, 2 Me), 2.94 (s, 6 H, 2 Me), 7.21–7.64 (m, 9 H, Ar and NH), 8.42 (NH); ^{13}C NMR (Me_2SO-d_6) δ 35.79 (2 Me), 36.08 (2 Me), 119.26 (2 C atoms), 124.03, 125.11, 126.96, 128.52 (2 C atoms), 129.59, 131.84, 135.15, 136.32, 139.74, 155.52 (C=O), 155.82 (C=O).

3,4′-Bis(*N′,N′*-dimethylureido)biphenyl (II). Approximately 25 mg (0.08 mmol) of 2-chloro-4′,5-bis(*N′,N′*-dimethylureido)biphenyl (Tanaka et al., 1981) was reductively photodechlorinated as described above for the 2,4′ isomer: mass spectrum *m/e* (rel intensity) 326 (M^+, 22), 281 (27), 236 (29), 72 (100), 44 (36); HPLC data given in Table I.

4,4′-Bis(*N′,N′*-dimethylureido)biphenyl (III). A slurry of 300 mg (1.17 mmol) of benzidine dihydrochloride (category I carcinogen) was neutralized with approximately 50 mL of 10 N sodium hydroxide. The free benzidine was extracted with ethyl acetate, and the extract was taken to dryness under reduced pressure. Dimethylcarbamoylation was conducted with 50 mL of acetonitrile, 10 mL of pyridine, and 15 mL of dimethylcarbamoyl chloride. The mixture was stirred under dark conditions under a nitrogen atmosphere for 16 h at ambient temperature in a fume hood. The reaction was then heated at reflux for 1 h, cooled in an ice bath, and treated with 2 N hydrochloric acid until gas evolution ceased. The product was extracted with ethyl acetate: mass spectrum *m/e* (rel intensity) 326 (M^+, 6), 281 (13), 236 (18), 133 (12), 89 (21), 72 (100), 45 (38); ^1H NMR (Me_2SO-d_6) δ 2.92 (s, 12 H, 4 Me), 7.49 (s, 8 H, Ar), 7.68 (s, H, NH), 8.30 (s, H, NH).

Hydrolysis of Fenuron Biphenyls. Fenuron biphenyls were obtained by photolyzing solutions (degassed with N_2) composed of monuron (200 mg) and fenuron (200 mg) dissolved in 1 L of acetonitrile–water (1:9). Mild conditions were necessary for hydrolysis because under the same conditions employed for monochlorobiphenyl hydrolysis (Tanaka et al., 1981), the fenuron biphenyls were completely decomposed to polar byproducts. About 100 mg of fenuron biphenyl was treated with 10 mL of ethanol and 5 mL of 6 N sodium hydroxide, and the reaction was heated at 90 °C under an atmosphere of nitrogen for 3 h. The product mixture contained polar decomposition products and hydrolyzed, half-hydrolyzed, and unhydrolyzed starting material according to analysis by TLC and HPLC. The freed amino moieties of the hydrolysis products were derivatized by refluxinng with acetic anhydride for about 1 h in ethyl acetate solution.

The major HPLC peak (C_{18} column) was 2,4′-bis(acetylamino)biphenyl: mass spectrum *m/e* (rel intensity) 268 (M^+, 89), 226 (98), 184 (100), 167 (14), 77 (7), 57 (10), 43 (92); ^1H NMR (Me_2SO-d_6) δ 2.94 (s, 6 H, 2 Me), 7.20 (d, H, J = 1.75 Hz), 7.25 (d, H, J = 1.75 Hz), 7.28 (s, 2 H), 7.40 and 7.49 (2 d, 4 H, J = 9.2 Hz, A_2B_2), 8.36 (s, NH), 9.16 (s, NH).

The minor HPLC peak (C_{18} column) was 4,4′-bis(acetylamino)biphenyl: mass spectrum *m/e* (rel intensity) 268 (M^+, 84), 226 (100), 184 (81), 167 (16), 77 (5), 57 (13), 43 (36).

Determination of Fenuron Biphenyl Pathways. Duplicate 2-mL aqueous samples were prepared as given below: (1) [^{14}C]fenuron (150 ppm, 0.82 μCi/mL); (2) [^{14}C]fenuron (75 ppm, 0.41 μCi/mL) and monuron (75 ppm); (3) [^{14}C]fenuron (75 ppm, 0.41 μCi/mL), monuron (75 ppm), and 0.2% Tergitol TMN-10 (w/v); (4) [^{14}C]-fenuron (75 ppm, 0.41 μCi/mL), monuron (75 ppm), and 0.2% Triton X-100 (w/v). All samples were handled in the same manner as described for the qualitative experiments. The biphenyls were separated from other reaction components by two-dimensional TLC using benzene–acetone (2:1) as the initial developing solvent and ether–hexane–pentane–acetic acid (40:5:5:2) as the final developing solvent. The biphenyl spot was removed from the TLC plates and assayed by LSC (Table II).

Isomeric Fenuron Biphenyl Distribution. Aqueous monuron (500 mL) under varying solution conditions was prepared as given below, and all samples were degassed with nitrogen: (1) monuron (180 mg/L); (2) monuron (180

Table II. Detection of Crossed Product Formation from Monuron Photocoupling with Fenuron[a]

expt[b]	% [^{14}C]-fenuron recovered	% [^{14}C]-biphenyls	% total ^{14}C recovered
I	100	0	100
II	86	5	96
III	97	2	100
IV	95	2	99

[a] Endogenous formation of fenuron was not taken into consideration. [b] I = [^{14}C]fenuron; II = [^{14}C]fenuron and monuron; III = [^{14}C]fenuron, monuron, and Tergitol TMN-10; IV = [^{14}C]fenuron, monuron, and Triton X-100.

Table III. Fenuron Biphenyl Distribution from Photolysis of Aqueous Monuron under Different Solution Conditions

samples[a]	% isomer distribution ortho	meta	para
monuron	62	5	33
monuron in 0.1 M NaOH	63	7	30
monuron in 0.2% TMN-10	91	2	7
monuron + fenuron (1:1.2 M)	75	tr[b]	25
monuron + fenuron (1:5 M)	77	tr	23
monuron + fenuron (1:1.2 M) in 0.2% TMN-10	89	1	10

[a] Samples were degassed with nitrogen. [b] Trace is approximately 0.1%.

mg/L) in 0.1 M NaOH; (3) monuron (180 mg/L) in 0.2% TMN-10 (w/v); (4) monuron (100 mg/L) and fenuron (100 mg/L) (1:1.2 M); (5) monuron (40 mg/L) and fenuron (164 mg/L) (1:5 M); (6) monuron (100 mg/L), fenuron (100 mg/L), and 0.2% TMN-10. For each solution condition, the 500-mL sample was divided into 25 20-mL samples for photolysis. Samples were irradiated for 135 min, and the isomeric biphenyls were isolated by preparative TLC. Separation and quantitation by HPLC were conducted with the CN and C_{18} Radial-Pak columns (Tables I and III).

Inhibition of Biphenyl Formation. Samples were prepared by dissolving [*ring*-^{14}C]monuron (1 mCi/mmol) into aqueous solutions of the inhibitors. Monuron concentration was 0.76 mM (150 ppm) and inhibitor concentration was 0.1 M. For all experiments, quadruplicate 2-mL samples were prepared, degassed with nitrogen, temperature equilibrated, and irradiated for 135 min. Quantitation of major products was performed by measuring the radioactivity by LSC for each product after separation by two-dimensional TLC (Tanaka et al., 1977).

Inhibitors surveyed qualitatively for effects on biphenyl formation were potassium cyanide, sodium hydroxide, isopropylamine hydrochloride, methanol, acetonitrile, nitromethane, piperidine, and pyridine. Quantitation of major products was determined for sodium hydroxide, isopropylamine hydrochloride, potassium cyanide, piperidine, and pyridine inhibition reactions (Table IV).

4-(Cyanophenyl)-1,1-dimethylurea (IV). Into a flask was added 295 mg (2.5 mmol) of 4-cyanoaniline, 10 mL of acetonitrile, 0.4 mL (5 mmol) of pyridine, and 1.5 mL (16 mmol) of dimethylcarbamoyl chloride. The reaction was heated for 24 h at 100 °C in an oil bath. The product was purified by preparative TLC and HPLC: mass spectrum *m/e* (rel intensity) 189 (M^+, 54), 144 (5), 72 (100), 43 (21), 40 (13); ^{1}H NMR (acetone-d_6) δ 3.01 (s, 6 H, 2 Me), 7.58 and 7.76 (2 d, 4 H, J = 9.2 Hz, A_2B_2), 8.17 (br s, H, NH).

4-(2-Pyridyl)nitrobenzene and 4-(3-Pyridyl)nitrobenzene. Nitration was accomplished by using 1 mL (7 mmol) of phenylpyridine, 3 mL of concentrated nitric acid, and 3 mL of concentrated sulfuric acid. After thorough agitation, the mixture was allowed to stand overnight. Workup was accomplished by pouring the acidic mixture onto crushed ice, making the reaction basic with 6 N sodium hydroxide, and isolating the precipitated product by filtration. Data for 4-(2-pyridyl)nitrobenzene are as follows: recrystallized from ethanol; mp 125–126 °C [lit. mp 130–131 °C (Katritzky and Simmons, 1960)]; mass spectrum *m/e* 200 (M^+); ^{1}H NMR (acetone-d_6) δ 7.44 (br s, H), 8.04 (m, 2 H), 8.37 (s, 4 H, Ar), 8.75 (d, H, J = 4 Hz). Data for 4-(3-pyridyl)nitrobenzene are as follows: recrystallized from ethanol; mp 147 °C [lit. mp 147–148 °C (Katritzky and Simmons, 1960)]; mass spectrum *m/e* 200 (M^+); ^{1}H NMR (acetone-d_6) δ 7.54 (2 dd, H, J = 4.8 Hz, J = 0.9 Hz), 8.02 and 8.38 (2 d, 4 H, J = 9.0 Hz, A_2X_2), 8.17 (dt, H, J = 4.8 Hz, J = 1.8 Hz), 8.68 (dd, H, J = 4.8 Hz, J = 1.8 Hz), 8.99 (d, H, J = 1.8 Hz).

4-(2-Pyridyl)aminobenzene and 4-(3-Pyridyl)-aminobenzene. To 0.7 g (3.5 mmol) of pyridylnitrobenzene was added to 10 mL of ethanol, 6 mL of 12 N hydrochloric acid, and 3.2 g of stannous chloride dihydrate. The reaction mixture was stirred for 1.5 h at 80 °C. The reaction was made basic with 6 N sodium hydroxide and extracted with benzene, and the extract was dried over anhydrous potassium carbonate. The product was precipitated from solution with an excess of dry hydrogen chloride. Data for 4-(2-pyridyl)aminobenzene are as follows: recrystallized from 2-propanol; mp 90–91 °C [lit. mp 96–97.5 °C (Katritzky and Simmons, 1960)]; mass spectrum *m/e* 170 (M^+); ^{1}H NMR (acetone-d_6) δ 4.87 (br s, 2 H, NH_2), 6.74 and 7.88 (2 d, 4 H, J = 8.8 Hz, A_2B_2), 7.12 (dd, J = 8.8 Hz, J = 4.8 Hz), 7.71 (dd, 2 H, J = 3.5 Hz, J = 1.3 Hz), 8.54 (d, H, J = 4.8 Hz). Data for 4-(3-pyridyl)aminobenzene are as follows: without further purification; mp 116–117 °C [lit. mp 118–120 °C (Katritzky and Simmons, 1960)]; mass spectrum *m/e* 170 (M^+); ^{1}H NMR (acetone-d_6) δ 4.86 (br s, 2 H, NH_2), 6.79 and 7.43 (2 d, 4 H, J = 8.8 Hz, A_2B_2), 7.33 (dd, H, J = 7.9 Hz, J = 4.8 Hz), 7.89 (dt, H, J = 7.9 Hz, J = 1.8 Hz), 8.43 (dd, H, J = 4.8 Hz, J = 1.8 Hz), 8.79 (d, H, J = 1.8 Hz).

Table IV. Inhibition of Biphenyl Formation in Aqueous Monuron Photolysis

inhibitor[a]	monuron, % decomposed[b]	major product(s) (% yield)[c]
NaOH	52	fenuron (7), fenuron biphenyls (8), fenuron triphenyls (6), polymers (8)
isopropylamine hydrochloride	52	fenuron (21), fenuron biphenyls (6), fenuron triphenyls (4), polymers (13)
piperidine	52	fenuron (43)
KCN	40	3-(4-cyanophenyl)-1,1-dimethylurea (30)
pyridine	33	4-(3-pyridyl)(*N'*,*N'*-dimethylureido)benzene (23)

[a] Inhibitor concentration was 0.1 M. [b] Irradiation time was 135 min. [c] Yields were based on the initial concentration of monuron.

4-(2-Pyridyl)(*N'*,*N'*-dimethylureido)benzene (V) and 4-(3-Pyridyl)(*N'*,*N'*-dimethylureido)benzene (VI). The hydrochloride salt of pyridylaminobenzene (0.5 g, 2.4 mmol) was dissolved in 25 mL of peroxide-free dioxane (Fieser and Fieser, 1967) in an apparatus (Shriner et al., 1943) for phosgene treatment. The dimethylcarbamoylation reaction with phosgene and dimethylamine was conducted as decribed earlier (Tanaka et al., 1981). Data for the 2-pyridyl isomer (V) are as follows: mass spectrum *m/e* (rel intensity) 241 (M^+, 30), 196 (35), 168 (9), 141 (22), 72 (100), 44 (76); ^{1}H NMR (acetone-d_6) δ 3.03

(s, 6 H, 2 Me), 7.26 (br m, H, NH), 7.68 and 8.03 (2 d, 4 H, J = 8.8 Hz, A_2B_2), 7.77–7.94 (m, 3 H), 8.63 (d, H, J = 4.7 Hz).

The initial purification of the 3-pyridyl isomer was by TLC using a solvent of benzene–acetone (2:1), R_f = 0.15. Final purification was by TLC in isopropyl ether–acetone (7:3) using four successive developments. The upper band that exhibited a blue fluorescence under ultraviolet light was the desired product. Data for the 3-pyridyl isomer (VI) are as follows: mass spectrum m/e (rel intensity) 241 (M^+, 100), 196 (68), 168 (16), 142 (15), 72 (100), 46 (71), 43 (49); ^{1}H NMR (acetone-d_6) δ 3.02 (s, 6 H, 2 Me), 7.41 (dd, H, J = 4.8 Hz), 7.57 and 7.72 (2 d, 4 H, J = 9.2 Hz, A_2B_2), 7.89 (br s, H), 8.02 (dt, H, J = 8.3 Hz, J = 1.8 Hz), 8.52 (br d, H, J = 3.8 Hz), 8.85 (s, H).

RESULTS AND DISCUSSION

Identification of Fenuron Biphenyls. After the identification of the two chlorinated bis(dimethylureido)biphenyls from the photolysis of monoron (Tanaka et al., 1981), further investigation was conducted to identify the corresponding photodechlorinated biphenyls observed in the photolysis of monuron in nonionic surfactant solutions (Tanaka et al., 1979). These fenuron biphenyls were initially characterized by their mass spectral molecular ion (m/e 326) and fragmentation pattern with two successive losses of mass 45 from the molecular ion. When monuron was photolyzed with sodium hydroxide or isopropylamine hydrochloride, fenuron biphenyls were also obtained. Although the partial characterization of these biphenyls was accomplished, the exact positions of the dimethylurea side chains were not clearly established.

Authentic standards of the three possible isomeric fenuron biphenyls were prepared from known starting materials. Acetylated analogues were also prepared as standards by the same method for comparison with the hydrolyzed and acetylated fenuron biphenyl photoproducts. The unkown biphenyl photoproducts were identified by chromatographic and spectroscopic comparison with the authentic standards as the 2,4′-bis(N',N'-dimethylureido)biphenyl (I, ortho coupled), 3,4′-bis(N',N'-dimethylureido)biphenyl (II, meta coupled), and 4,4′-bis(N',N'-dimethylureido)biphenyl (III, para coupled).

Pathways of Biphenyl Formation. Photodechlorination was generally the main reaction with solutions containing compounds with labile hydrogen. Consequently fenuron was produced in high yield under these conditions. In addition to the formation of fenuron, however, fenuron biphenyls were also observed in significant amounts. Three different pathways could be visualized for the formation of fenuron biphenyls in monuron photolysis (Figure 2). The expected pathway for fenuron biphenyl formation would be by photocoupling of two monuron molecules (pathway 1) to yield chlorinated biphenyls that would then be dechlorinated to afford fenuron biphenyls. As a second possibility, two fenuron molecules could couple (pathway 2) during photolysis to form fenuron biphenyls. This pathway appeared attractive because the yields of fenuron from monuron photolysis were sometimes greater than 50% in the presence of nonionic surfactants (Tanaka et al., 1979). As the last possibility, photoexcited monuron could form a crossed product with fenuron (pathway 3) to produce fenuron biphenyls directly.

For determination of the pathway of fenuron biphenyl formation, two experiments were conducted. In the first, aqueous solutions of [^{14}C]fenuron were photolyzed to determine if photoexcited fenuron could couple with a second molecule of fenuron to afford the biphenyls via pathway 2. In the second set of experiments, an approximate 1:1 molar ratio of monuron and [^{14}C]fenuron was photolyzed with and without surfactant to determine if biphenyls could be produced under these conditions via pathway 3. The negative results in Table II for the first set of experiments clearly established that photocoupling of two fenuron molecules was not occurring. In the second set of experiments, a 5% yield of [^{14}C]fenuron biphenyl was produced as a crossed product in the absence of surfactant. A 2% yield of [^{14}C]fenuron biphenyl was obtained with addition of the two different surfactants. The observed reduction in [^{14}C]fenuron biphenyl yields with surfactant was primarily due to the dilution of the [^{14}C]fenuron specific activity by the endogenous formation of fenuron from monuron photodechlorination. The detection of the crossed product clearly established that photoexcited monuron reacts not only with other molecules of monuron but also with fenuron to afford fenuron biphenyls. Thus, in the presence of organic materials such as surfactants in aqueous solution, fenuron biphenyls can be produced by pathways 1 and 3 of Figure 2 and not by pathway 2 involving two fenuron molecules.

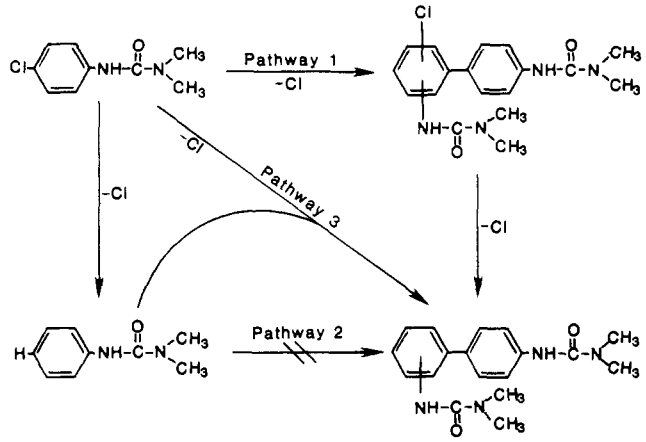
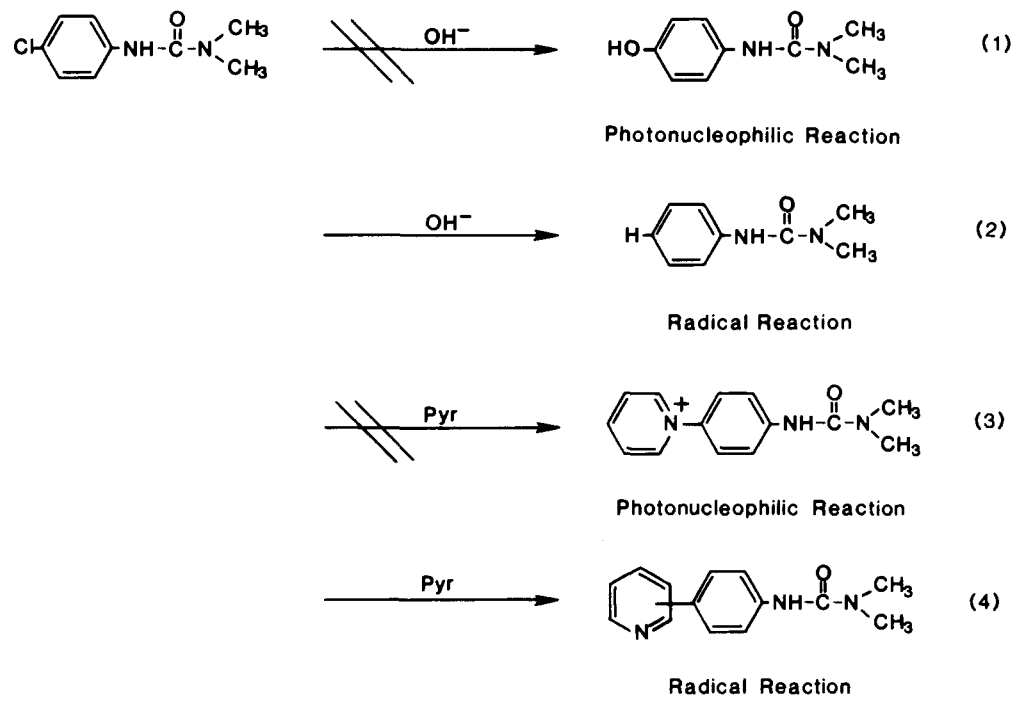


Figure 2. Scheme of the different pathways for fenuron biphenyl formation.

Isomeric Distribution of Fenuron Biphenyls. With the identification of the isomeric fenuron biphenyls, it was necessary to determine the distribution of the three isomers under different solution conditions to assist in the elucidation of the mechanism of the coupling process. Table III shows only the percent distribution of I, II, and III; therefore, a high percent isomeric distribution does not designate a high product yield. In previous studies with oxygenated systems (Tanaka et al., 1981), the isomeric ratio of the chlorinated biphenyls was 92% ortho and 8% meta coupled. In the current study with degassed systems, however, a significant amount of para coupling was observed under all conditions examined. With an appreciable amount of para coupling taking place, the data of Table III indicate that formation of I was occurring by pathways 1 and 3 of Figure 2. With the addition of fenuron into the reaction mixture, the formation of II was reduced to negligible quantities; hence, meta coupling was apparently occurring only by pathway 1. Para coupling to yield III could only occur by pathway 3 because the para position of monuron was blocked in pathway 1. The low yields of III obtained in the presence of surfactants indicate that pathway 1 was the predominant pathway under these conditions.

Inhibition Studies. Experiments were conducted to block biphenyl formation in order to gain some insight into the mechanism of biphenyl production. In these studies, aqueous monuron solutions at 0.76 mM concentration were photolyzed with selected inhibitors at 0.1 M concentration



(Table IV). When sodium hydroxide or isopropylamine hydrochloride was used as inhibitor, photoreduction was the major reaction, and photocoupling was the second most important reaction. There was no noticeable decrease in total biphenyl yields with these inhibitors. Methanol, acetonitrile, and nitromethane were also examined qualitatively as inhibitors. These compounds also caused photodechlorination and biphenyl coupling reactions to take place. In addition, acetonitrile formed cyanomethyl substitution products in small amounts with monuron on both the ring and side chain. Similarly, nitromethane gave evidence for ring substitution reaction by nitro and methyl oxime groups in very low yield. These photoproducts were partially characterized by mass spectral analysis.

With the addition of piperidine, photoreduction was the primary reaction, and yet biphenyl formation was completely inhibited, which was contrary to the results observed with hydroxide ion and isopropylamine. In the presence of potassium cyanide, the *p*-cyano substitution product (IV) was the major photoproduct, and only trace amounts of biphenyls could be detected. Pyridine afforded a *p*-pyridyl adduct with phenyldimethylurea as the major product, and again only trace amounts of biphenyls could be detected. Therefore, piperidine, cyanide ion, and pyridine efficiently trapped the active intermediate involved in biphenyl formation. Interestingly, cyanide ion and pyridine protected monuron against photodegradation as was demonstrated by the reduced level of monuron decomposition during a constant exposure period (Table IV).

Photonucleophilic substitution reactions were reported (Letsinger et al., 1965) for the photolysis of 4-nitroanisole in the presence of hydroxide ion. Under these basic conditions, either the nitro or the methoxyl group of 4-nitroanisole was displaced by hydroxide ion. In the presence of pyridine, however, only the nitro group was displaced and bonding with anisole occurred at the nitrogen atom of pyridine to afford a pyridinium salt.

With oxygen present in monuron photolysis, the para-hydroxylated analogue of monuron was the most abundant photoproduct identified (Tanaka et al., 1977). If oxygen was excluded, the para-hydroxylated material was only observed in trace quantities, thus suggesting the involvement of radical intermediates. Addition of hydroxide ion as shown in Table IV caused photoreduction to be the primary reaction rather than hydroxide ion substitution, which would be the expected result from photonucleophilic reaction (eq 1 and 2).

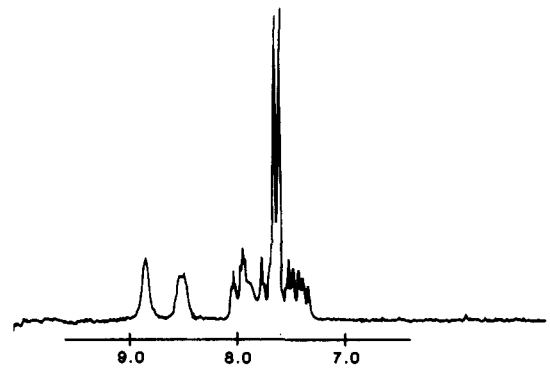


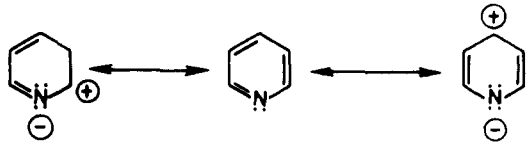
Figure 3. NMR spectrum of the aromatic region of 4-(3-pyridyl)(*N'*,*N'*-dimethylureido)benzene.

In the presence of pyridine, a pyridyl substitution product was obtained that gave a molecular ion at *m/e* 241, indicating that hydrogen chloride was a byproduct of the coupling process. Consequently, bonding of the phenyl ring with pyridine would be expected to be carbon–carbon rather than carbon–nitrogen. This result represents further evidence against a photonucleophilic reaction (eq 3 and 4).

The NMR spectrum of the aromatic region of the pyridyl substitution product is shown in Figure 3. The A_2B_2 pattern for para substitution on the phenyl ring shows that pyridine coupling is occurring at the para position of monuron. A doublet of triplets, an unresolved doublet, and a broad singlet are observed downfield from the phenyl protons. These peaks represent three protons by integration, and a fourth proton is observed upfield from the phenyl protons as a doublet of doublets. The NH proton of urea at δ 7.9 is seen as a broad shoulder on the upfield triplet of the doublet of triplets. Since the NMR spectrum shows the presence of four different protons on the pyridine ring, coupling must be occurring either at the α or at the β position of pyridine. Synthetic standards of V and

VI were prepared starting with α- and β-phenylpyridine. Upon spectroscopic comparison of the synthetic materials with the unknown, the β isomer (Figure 1, VI) was determined to be identical with the unknown photoproduct. Therefore, the coupling of photoexcited monuron with pyridine was occurring specifically at the β position.

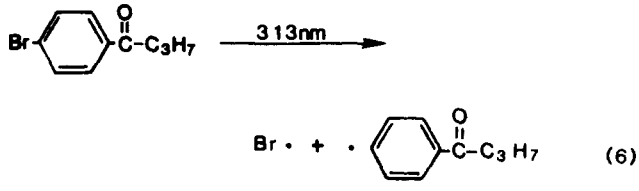
Mechanism of Biphenyl Formation. According to the valence-bond description of pyridine (Paquette, 1968), the zwitterionic forms are considered to contribute substantially to the hybridized bonding of pyridine (eq 5). Thus



(5)

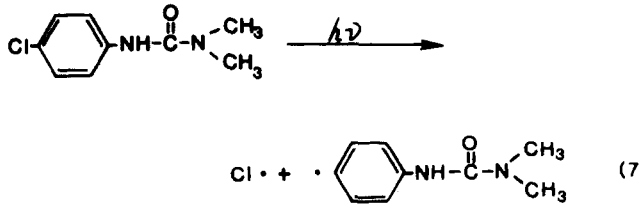
if a positively charged group was attacking pyridine, coupling would be expected to occur at the negatively charged nitrogen atom (Pryor, 1978). On the other hand, if the incoming group contained a negative charge, attack would be expected to take place at the more positively charged α or γ positions (Paquette, 1968). Therefore, in the photolysis of monuron, the excited specie that attacks pyridine was apparently a neutrally charged group.

Using electron spin resonance (ESR) spectrometry, Baum et al. (1966) observed an ESR signal for the butyrophenone radical during the photolysis of *p*-bromobutyrophenone owing to homolytic cleavage of the carbon–bromine bond (eq 6). On the basis of its absorption



(6)

spectrum, photolysis of *p*-bromobutyrophenone with 313-nm monochromatic light should effect excitation of only the carbonyl group. By use of 313-nm light, however, carbon–bromine bond cleavage was stilled observed, thus suggesting that absorbed energy was being transferred from the side chain to the site of bond cleavage on the aromatic ring. In the photolysis of monuron in methanolic solution under anerobic conditions, Mazzocchi and Rao (1972) observed a clean photodechlorination of monuron to fenuron. Photoreduction was suggested to take place via a mechanism involving dimethylphenylurea radicals formed from homolytic cleavage of the carbon–chlorine bond (eq 7).



(7)

Free radicals have been shown to add readily to aromatic systems (Walling, 1975), and biphenyls are prepared by free radical reactions (Bachmann and Hoffman, 1944; van Tamelen et al., 1965). There is very little evidence that displacement of groups other than hydrogen by phenyl radicals plays a significant role (Perkins, 1973). Therefore, the formation of free radicals by homolytic cleavage of the carbon–chlorine bond as suggested by Mazzocchi and Rao (1972) appears very attractive as the mechanism for the photodegradation of monuron. In our studies, the aryl free

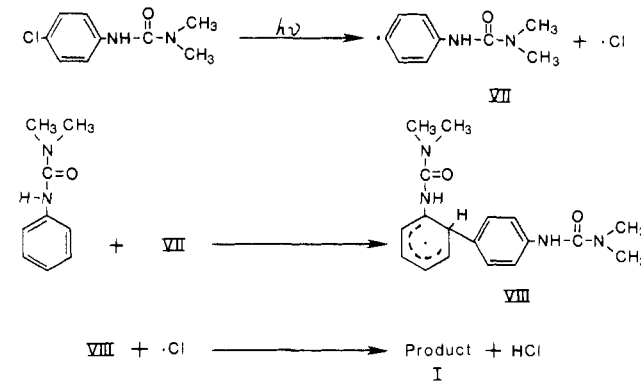


Figure 4. Scheme for the addition–elimination mechanism for biphenyl formation.

radical was trapped with cyanide ion to yield IV. Furthermore, the hydrogen abstraction reaction to yield fenuron was completely eliminated. These results are in good agreement with the capture of aryl radicals by cyanide ion as reported by Bartak et al. (1970). Therefore, the biphenyls from monuron photolysis are apparently being produced by a free radical reaction. The regioselectivity of radical coupling with monuron at the ortho position was 92%, with pyridine at the β position was 100%, and with fenuron at the ortho and para positions was 76 and 24%, respectively.

An attractive mechanism to account for the formation of biphenyls in this study appears to be the addition–elimination mechanism (Perkins, 1973) as shown in Figure 4. The *N*,*N*,-dimethylphenylurea radical (VII) is formed in the light-induced initiation step, and VII adds to the aromatic ring of fenuron to form a phenylcyclohexadienyl radical as the transition-state radical intermediate (VIII). In the transition state, considerable development of the new carbon to carbon bond is apparently occurring because of the high degree of selectivity observed in the coupling reaction (Perkins, 1973). Facile homolytic cleavage of the weakly bonded hydrogen from VIII, perhaps by chlorine abstraction, would then afford the product in the termination step.

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Pyrethroid Photochemistry: Intramolecular Sensitization and Photoreactivity of 3-Phenoxybenzyl, 3-Phenylbenzyl, and 3-Benzoylbenzyl Esters

Luis O. Ruzo* and John E. Casida

Intramolecular sensitization is examined as a means to modify pyrethroid photostability by using a series of 3-phenoxybenzyl (**A**), 3-phenylbenzyl (**B**), and 3-benzoylbenzyl (**C**) esters of *cis*-chrysanthemic acid (**1**), *cis*-3-(2,2-dichloro- and -dibromovinyl)-2,2-dimethylcyclopropanecarboxylic acids (**2** and **3**), 2,2,3,3-tetramethylcyclopropanecarboxylic acid (**4**), and α-(4-chlorophenyl)isovaleric acid (**5**). Quantum yields in degassed benzene solutions irradiated at 300 nm are similar for **A** and **B** esters, whereas remarkable stability is encountered with **C** esters of **4** and **5** as a result of decreased ester cleavage, a reaction that proceeds by direct absorption rather than via triplet states populated by energy transfer. Esters of **C** with **1**, **2**, and **3** undergo greatly enhanced cis/trans isomerization due to intramolecular energy transfer. On exposure of thin films to sunlight the stability order is generally **A** > **B** > **C** as expected from their absorptivity and **4** > **5** > **2** > **3** > **1**, consistent with their absorptivity and ease of oxidation. Sunlight irradiation of **2** and **3** esters yields the trans isomers and ester cleavage materials as major products and the monohalovinyl derivatives and the caronaldehyde and caronic acid esters as minor products. The **C** moiety is stabilized to light without destroying the insecticidal activity on derivatization as the benzhydryl acetate.

Photostability is an important consideration in the design and use of pyrethroids for agricultural pest control. Photolabile substituents have been replaced with isosteric groups resistant to oxidation and other photoreactions, thereby conferring enhanced stability (Ruzo, 1982; Ruzo and Casida, 1980). Photoreactions might also be minimized by introducing substituents for radiative energy disposal or for intramolecular transfer of absorbed energy to nonreactive groups.

The photolability of chrysanthemates (**1**, Figure 1) is due in part to the ease of oxidation at the isobutenyl methyl group and double bond (Chen and Casida, 1969; Ruzo et al., 1980, 1982) that has been overcome by replacing the isobutenyl acid with dihalovinyl acids **2** and **3** [e.g., permethrin (**2A**) is much more stable than phenothrin (**1A**) (Elliott et al., 1973; Ruzo and Casida, 1980)]. Esters of **1** readily undergo cis/trans photoisomerization in the presence of acetophenone (E_t = 74 kcal/mol) and benzophenone (E_t = 69 kcal/mol) (Ruzo et al., 1982; Ueda and Matsui, 1971). Known photoreactions of esters derived from **2** and **3** are dominated by cis/trans isomerization and do not include oxidation of the dihalovinyl substituent (Holmstead et al., 1978a; Ruzo et al., 1977). Acid moiety **4**, present in fenpropathrin (Matsuo et al., 1976), is of interest because photochemical cleavage of the C1–C3 bond may yield a diradical that can recombine to regenerate the starting cyclopropanecarboxylate. Photodegradation of fenvalerate and analogues derived from acid moiety **5** is characterized by extensive decarboxylation (Holmstead et al., 1978b).

The phenoxybenzyl moiety (**A**) and its α-cyano analogue are present in the major pyrethroids permethrin, cypermethrin, deltamethrin, and fenvalerate. Phenylbenzyl and benzoylbenzyl moieties **B** and **C** also yield insecticidal esters, e.g., **2B** (Plummer and Pincus, 1981) and **2C** (Elliott and Janes, 1979; Plummer and Pincus, 1981). The biphenyl (E_t = 65 kcal/mol) and benzophenone chromophores in these compounds have triplet energies sufficient to profoundly influence cis/trans isomerization, decarboxylation, and ester cleavage reactions.

This study evaluates the effects of sensitizing chromophores on the photoreaction rates and photoproducts of a variety of pyrethroids derived from acid moieties **1**–**5** and alcohol moieties **A**–**C** (Figure 1).

MATERIALS AND METHODS

Chromatography and Spectroscopy. Thin-layer chromatography (TLC) utilized silica gel F-254 chromatoplates with 0.25- and 0.5-mm gel thickness for analytical and preparative purposes, respectively, and compound detection by quenching of gel fluorescence at 254 nm. High-pressure liquid chromatography (HPLC) was carried out on a μPorasil column (30 cm × 7.8 mm i.d.) eluted with chloroform–hexane (3:1) at 1–2 mL/min. UV absorption spectra were determined for compounds in chloroform solution.

Analysis. Gas–liquid chromatography (GLC) was accomplished in four systems: (A) an SP-2100 capillary column (Supelco, Bellefonte, PA) with helium carrier gas or (B) an OV-101/OV-210 (3% each) packed glass column with argon–methane (20:1) carrier gas, in each case in conjunction with a Hewlett-Packard 5840 chromatograph with ^{63}Ni electron capture detector and on-line computer to calculate retention times (R_t) and normalized peak areas; (C) a 5% OV-25 packed glass column with nitrogen carrier gas and a Varian Aerograph 1400 instrument with a flame ionization detector; (D) a 5% OV-101 column with methane as the carrier and ionization gas at 0.8 torr in conjunction with a Finnigan 9500 chromatography, a Finnigan

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