The energy requirements and the ease of operation must be considered in comparing the use of an alcohol with that of a ketone in the purification of wet-process phosphoric acid. The stripping with water, concentration of purified acid, and recovery of the solvent alcohol should be compared with the simultaneous distillation of ketone and concentration of the purified acid. Final evaluation of the two different processes should be made on the basis of results of tests on a larger than laboratory scale.

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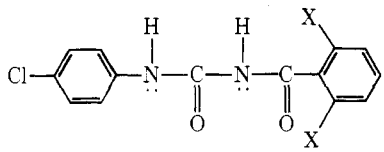
Photochemistry of Bioactive Compounds. 1-(4-Chlorophenyl)-3-(2,6-dihalobenzoyl)ureas

Luis Octavio Ruzo, Matthew J. Zabik,* and Robert D. Schuetz

The photoproducts obtained upon irradiation at 300 nm of 1-(4-chlorophenyl)-3-(2,6-dichlorobenzoyl)urea (I) and 1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea (II) in methanol solution and in the solid phase were identified. Photolysis of I yielded *p*-chlorophenyl isocyanate, *N*-4-chlorophenyl methylcarbamate, *N*-phenyl methylcarbamate, 2-chlorobenzamide, and 2,6-dichlorobenzamide. The photoproducts of II were identified as *p*-chlorophenyl isocyanate, *N*-4-chlorophenyl methylcarbamate, *N*-phenyl methylcarbamate, and 2,6-difluorobenzamide. Mechanistic pathways are examined and discussed. The possibility of a type II disproportionation is considered.

The photochemistry of urea-based herbicides has received considerable attention recently (Mazzochi and Rao, 1972; Crosby and Tang, 1969). The major reaction pathways observed involve either photodechlorination or carbamate formation in the presence of methanol. When water is used as solvent hydration products have been detected (Rosen *et al.*, 1969).

It was of interest to determine the photoproducts arising from systems containing more than one amide bond. 1-(4-Chlorophenyl)-3-(2,6-dichlorobenzoyl)urea (I) and 1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea (II) were chosen for study since both the reactivities of the halogen and amide bonds could be studied.



I, X = Cl
II, X = F

The Pesticide Research Center and the Departments of Chemistry and Entomology, Michigan State University, East Lansing, Michigan 48824.

EXPERIMENTAL SECTION

Materials. Compounds I and II were obtained from Thompson-Hayward Chemical Co. (Kansas City, Kan.) under the designations TH 6038 and TH 6040, respectively. The samples were purified by recrystallization from methanol and acetone until pure by thin-layer chromatography (tlc).

Standards. 2,6-Dichlorobenzamide, 2-chlorobenzamide, 4-chlorophenyl isocyanate, and phenyl isocyanate were obtained from Aldrich Chemical Co. and used without further purification. *N*-*p*-Chlorophenyl and *N*-phenyl methylcarbamates were prepared by refluxing the respective isocyanates in methanol for 6 hr. This method gave a >90% yield of the methylcarbamates.

All samples prepared or commercially obtained were authenticated by gas chromatography (gc) and/or mass spectrometry.

Solvents. The methanol used in the photoreactions was obtained from Mallinckrodt Chemical Works in Spectrophotometric Grade. The methanol, benzene, and acetone used as tlc or extraction solvents were glass distilled (Burdick and Jackson Laboratories, Muskegon, Mich.).

Photochemical Equipment. All photolyses were carried out in a Rayonet Photochemical Reactor (The Southern New England Ultraviolet Co.) fitted with RUL 3000 lamps having a peak energy output at 300 nm. During irradia-

Table I. Photoproducts of 1-(4-Chlorophenyl)-3-(2,6-dihalobenzoyl)ureas (I and II) in Methanol

	% yield	R_t, min	R_f	Parent (M^+)
Photoproducts of I				
4-Chlorophenyl isocyanate (Ia)	<1	1.1		153
N-Phenyl methylcarbamate (Ib)	39	1.9	0.61	151
2-Chlorobenzamide (Ic)	<1	3.2		155
N-(4-Chlorophenyl) methylcarbamate (Id)	10	4.7	0.47	185
2,6-Dichlorobenzamide (Ie)	49	7.5	0.35	189
Photoproducts of II				
4-Chlorophenyl isocyanate (IIa)	<1	1.1		153
N-Phenyl methylcarbamate (IIb)	45	1.9	0.61	151
2,6-Difluorobenzamide (IIc)	49	2.3	0.31	157
N-(4-Chlorophenyl) methylcarbamate (IId)	4	4.7	0.47	185

tion the samples were contained in Teflon-stoppered borosilicate glass tubes (13 × 100 mm) with a minimum uv cutoff at 285 nm. Solid phase photoreactions were carried out on silica gel plates. The irradiation chamber temperature was 30–40°. A "merry-go-round" arrangement was employed to ensure equal exposure of all samples to uv irradiation.

Analytical Equipment. Gc analyses were performed on a Beckman GC-65 apparatus equipped with flame ionization detector and a 6 ft × ⅛ in. i.d. glass column packed with 4% SE-30 on Gas Chrom Q (80–100 mesh). The helium carrier gas flow was 40 ml/min. The column oven was maintained at 170°. Detector and inlet temperatures were 280 and 250°, respectively. The gas chromatograph was interfaced with a Du Pont 21-490 mass spectrometer interfaced with a PDP-12-LDP computer (Digital Equipment Corp.).

Ultraviolet spectra of I and II were taken in methanol using a Beckman DB-G grating spectrophotometer. Qualitative tlc was done on precoated 0.25-mm silica gel plates containing F-256 fluorescent indicator (E. Merck reagents). Preparative tlc plates were prepared with silica gel GF254 (2 mm). The developing solvent was an 80:20 benzene–methanol mixture.

RESULTS AND DISCUSSION

Photochemical Procedures. *Product Identification.* Fifty-milliliter aliquots of solutions of I and II in methanol (0.01 *M*) were irradiated for periods of 50–80 hr. After reaction the samples were evaporated to dryness and the residue dissolved in acetone. Tlc was achieved by running 10-μl spots. After band separation and extraction with acetone each sample was injected in the gc–mass spectrometer. Direct injection, without prior tlc separation, yielded the same number of components. Gc retention times (R_t), R_f values, and mass/charge ratios of the parent peaks (M) of all photoproducts (a–e) are shown in Table I. The values obtained match those of authentic standards. Reaction paths are outlined in Schemes I and II. Photolysis of I at either pH 4 or 9 gave the same products in slightly higher yields than those obtained in the absence of acid or base. Solid phase reaction of I afforded only Ia and Ie after 80 hr of irradiation.

Photolysis of Ia in methanol yielded Ib and Ic after 25 hr. Photoproduct Ie was found to be uv stable for up to 60 hr of irradiation in methanol at 300 nm. Compounds I and II were found to be stable in the dark over comparable time periods.

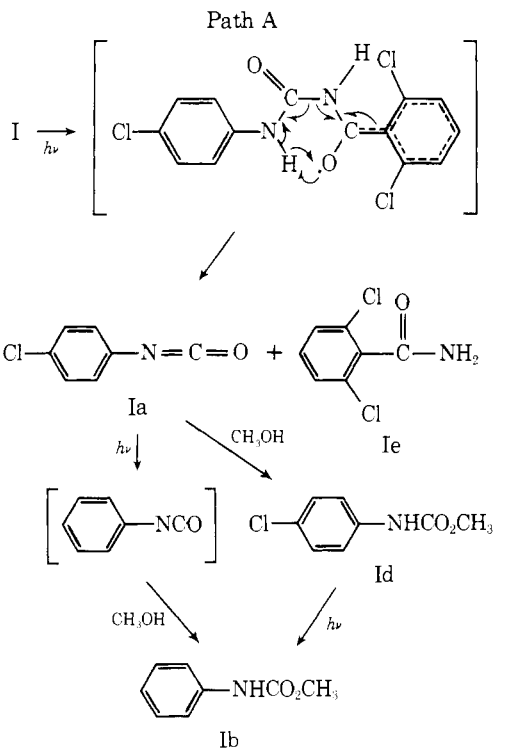
Product Yields. The yield of each product arising from I and II was calculated from a standard curve prepared from the gc areas of at least four concentrations of authentic material. The yield of Ia and Ic was only estimated due to their very low concentration. All yields were calculated after 65 hr of irradiation and are given as the per cent of total product formation (Table I). After this time period 20% of I and 12% of II had reacted. Photolysis of I in benzene yielded only Ia and Ie as major products.

Mass Spectrometry. Product Ia showed a parent peak (M) at *m/e* 153, main signals at 155 (M + 2), 125 (M − CO), and 90 (M − CO − Cl). Gc and tlc analyses showed it to be identical with IIa. Product Ib had M at *m/e* 151 with main fragments at 119 (M − CH_3OH) and 92 (M − CO_2CH_3). Ib and IIb were identical compounds.

Compound Ic had M at *m/e* 155 with main fragments at 157 (M + 2), 139 (M − NH_2), and 111 (M − $CONH_2$). Product Id (M at 185) showed fragments at *m/e* 187 (M + 2), 155 (M − CH_3OH), 126 (M − CO_2CH_3), and 91 (M − CO_2CH_3 − Cl). Id and IId were identical. Product IIc had M at *m/e* 157 and fragments at 141 (M − NH_2) and 113 (M − $CONH_2$). Product Ie had M at *m/e* 189 with M + 2 and M + 4 at 191 and 193. Fragments appeared at 173 (M − NH_2), 145 (M − $CONH_2$), and 110 (M − $CONH_2$ − Cl).

Mechanism. Compounds I and II absorb in the 280–320-nm region with extinction coefficients in the order of 10^3. The first absorption band of aliphatic amides occurs

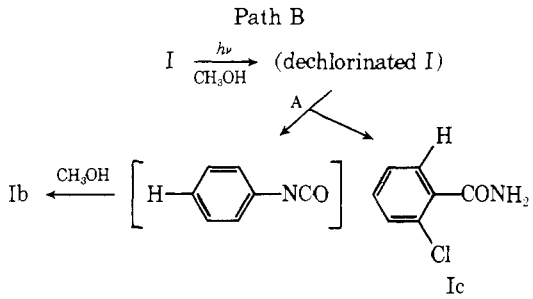
Scheme I



with ϵ in the order of 10^2. The increased value observed for I and II implies an allowed transition involving the phenyl group α to the carbonyl. In aliphatic amides the photodissociative step involves type II fragmentation to the enol (Calvert and Pitts, 1966). Compounds I or II could presumably undergo a similar process. The result is then path A (Scheme I) which can occur without formation of "free radicals." Furthermore, conjugative affects imply that the excitation will occur at that carbonyl group. This type of an excited state has been described by Stenberg (Stenberg and Dutton, 1972). Absence of free radicals is justified in that in the photolysis of I in benzene, products Ia and Ie were predominant even though benzene is a very poor hydrogen donor.

Products from path B (Scheme II) have been observed with other chloro aromatic amides and dechlorination to form Ib and Ic has been substantiated (Elad *et al.*, 1965; Reisch and Niemeyer, 1968). Methylcarbamates have also been observed to arise from isocyanates in methanol (Mazzochi and Rao, 1972).

Scheme II



We have found the dechlorination step to occur when pure Id was photolyzed in methanol. We have also found that Ia forms Id in the dark in >90% yield. Solutions of 2,6-dichlorobenzamide in methanol were found to be uv stable up to 60 hr of irradiation; dechlorination from the ortho position of I must therefore occur prior to C–N cleavage. No defluorination products from II were observed. This is in agreement with evidence of greater reactivity down the sequence F < Cl < Br < I. The slightly enhanced photodecomposition of I in acid or base supports the intermediacy of enol-like excited states or intermediates. Oxygen saturated solutions of I showed no rate decrease suggesting that the reaction does not proceed *via* a long-lived triplet excited state.

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Fenfluramine Residues in Chickens and Eggs

Robert B. Bruce,* William R. Maynard, Grover D. Cloyd, and Donald L. Gilbert

The disappearance of fenfluramine, [*N*-ethyl-α-methyl-*m*-(trifluoromethyl)phenethylamine] hydrochloride, an anorexigenic agent, from chicken tissues and eggs was established. No detectable residue of fenfluramine or its deethylated metabolite (norfenfluramine) could be found, following administration of 300 g/ton of feed, after 6 days in the eggs and after 2 days in the tissues, following withdrawal of the drug.

Fenfluramine, [*N*-ethyl-α-methyl-*m*-(trifluoromethyl)-phenethylamine] hydrochloride, has found extensive use as a very effective anorexigenic agent showing little or no CNS stimulant properties in humans and lower animals (Franko *et al.*, 1965). The present study was undertaken as part of an investigation to determine whether fenfluramine would be a useful agent for the control of weight in broiler breeders. Broiler breeder hens in contrast to layer breeders are selected and are genetically elegant to produce fat, fast gaining heavy birds. This body condition of obesity reduces egg production and longevity. By maintaining broiler breeders in a lean, trim condition through limitation of feed intake you obtain higher egg production and a longer productive life. This is not possible by simply limiting the feed allowed because birds eat litter, each other, and anything else available. In an unpublished part of this investigation (Gilbert, 1971) it had been shown that fenfluramine was effective in weight reduction, and did not give toxic effects nor affect egg production. The study reported here was undertaken to show the maximum concentrations of fenfluramine that may be found in tissues and eggs, and to determine the rate of disappearance of the drug following the feeding of an effective dose to chickens.

The metabolism of fenfluramine in lower animals and man has previously been reported (Duhault and Fenard, 1965; Beckett and Brookes, 1964; Bruce and Maynard, 1968). The main metabolic products are deethylated fenfluramine, α-methyl-*m*-(trifluoromethyl)phenethylamine (norfenfluramine), and *m*-trifluoromethylhippuric acid. Since norfenfluramine might be expected to show similar activity to fenfluramine, it was also determined in this study.

EXPERIMENTAL SECTION

Analytical Methods. The analytical method previously reported for determining urine concentrations (Bruce and Maynard, 1968) was adapted for use in this study. The gas chromatograph was a Barber-Colman with flame ionization detectors. The ⅛ in. stainless steel column was 6 ft long with 10% Carbowax 20M and 5% KOH on Gas-Chrom Q and was operated at 120°. The injector and detector temperatures were 260°, and the nitrogen flow rate was 30 ml/min.

A. H. Robins Co., Research Laboratories, Richmond, Virginia 23220.