Original Article

Production of Benzamide and Isoindoline Type Compounds on Photodegradation of Benzanilides

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Mepronil (3'-isopropoxy-2-methylbenzanilide) produces *o*-toluamide on silica gel and 1hydroxy-3-oxo-2-(3'-isopropoxyphenyl)isoindoline in water when irradiated with sunlight and ultraviolet rays. These types of photoreaction were found to be common in other substituted benzanilides. Degradation rate of 3'-methoxy-2-substituted benzanilides when irradiated with ultraviolet rays on silica gel plate was affected by the *o*-substituent.

INTRODUCTION

Mepronil has a strong fungicidal activity especially against rice sheath blight fungus (Rhizoctonia solani Kühn). To evaluate its ecotoxicological safety, the fates in soils¹⁾ and plants²⁾ and under lights³⁾ have been studied. Interestingly the main product of mepronil on silica gel chromatoplate exposed to sunlight was o-toluamide, whereas the main product in water irradiated with ultraviolet ray was 1-hydroxy-3-oxo-2-(3'-isopropoxyphenyl) iso-In this study, various substituted indoline. benzanilides (I) (Fig. 1) were submitted to such conditions to know the generality of these types of photoreaction.

MATERIALS AND METHODS

1. Chemicals

The synthesis of benzanilides and related compounds used in this study were reported elsewhere.⁴⁾ The properties of these compounds are shown in Table 1.

2. Photodegradation of Benzanilides 2.1 On silica gel

In a 100 ml round bottomed flask, a mix-

ture of 3.3×10^{-5} mol of each benzanilide (I: X=Me, MeO, Cl, NO₂, CF₃ or H; Y=3'-MeO or 3'-i-PrO) and 1.7×10^{-5} mol of xanthone as photosensitizer was dissolved in 30 ml of dichloromethane. Ten grams of silica gel C-200 (Wako Pure Chem.) was added to the flask and concentrated under reduced pressure, then dried in a vacuum desiccator containing calcium chloride and Ascarite II (Arthur H. Thomas Co.) for one day. In a petri dish, 3 g of the above silica gel powder inpregnating each benzanilide and a small cup which contains 500 mg of Ascarite were placed. The Ascarite was used to absorb CO_2 evolved, if any, by the photodegradation. The whole petri dish was sealed tightly with a thin film of polychlorovinylidene (Krewrap, Kureha Chem., Ind.). Benzanilide on silica gel powder was exposed to sunlight for 10 days during June season in 1982. The silica gel powder was extracted with 50 ml of acetonitrile and analyzed by HPLC. Silica gel powder containing xanthone was also exposed to sunlight for estimation of CO_2 evolved from this origin.

2.2 On silica gel plate

One mg of each benzanilide was dissolved in

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Compound	mp (°C)	Retention time	Rf va	ulue ^{a)}
Compound		(min) of HPLC	A	В
Benzanilides		Ann Anna Anna Anna Anna Anna Anna Anna		
3'-i-PrO-2-Me	92-93	6.06	0.79	0.74
3'-MeO-2-Me	146–147	2.97	0.67	0.75
3'-MeO-2-MeO	171-173/0.01 ^b)	4.05	0.63	0.80
3'-MeO-2-Cl	139–140	2.88	0.57	0.64
3'-MeO-2-CF ₃	109–110	3.07	0.56	0.66
3'-MeO-2-NO ₂	154-156	1.90	0.21	0.35
3′-MeO-2-H	110-111	2.61	0.54	0.61
2′-MeO-2-Me	80- 81	4.64	0.81	0.82
4'-MeO-2-Me	142–143	2.48	0.59	0.60
H-2-Me	127-128	2.88	0.70	0.69
Benzamides				
2-Me	141–142	0.58	0.16	0.12
2-MeO	122-124	0.67	0.18	0.21
2-Cl	142-143	0.60	0.16	0.13
2-CF ₃	162-163	0.63	0.24	0.12
$2-NO_2$	172-173	0.47	0.05	0.05
H	125-126	0.49	0.11	0.08
Benzoic acids				
2-Me	130-135	4.09°)		
2-MeO	98–100	1.18°)		
2-Cl	138-140	3.34°)		
2-CF ₃	111-113	3.75°)		
Н	122–123	1.95°)		
1-Hydroxy-3-oxo-2-(sul	ostd•phenyl)isoindolines			
3'-i-PrO	143-144	2.27	0.46	0.36
2'-MeO	166–167	0.95	0.17	0.17
3'-MeO	125-126	1.27	0.32	0.30
4'-MeO	152-154	1.05	0.26	0.24
Н	167-169	1.14	0.37	0.30

Table 1 Properties of benzanilides and related compounds.

^{a)} A: n-hexane/dioxane (2/1), B: benzene/methanol (19/1).

^{b)} bp (°C/mmHg), ^{c)} as methyl ester.

2 ml of acetone and adsorbed onto 4×10 cm silica gel chromatoplate (precoated without fluorescent indicator, 20×20 cm, 0.25 mm thickness, E. Merck) using a pipet. The chromatoplate was irradiated under high-pressure mercury lamp (the maximum intensity at 365 nm, 400 W) from the distance of 10 cm for 20 hr. The silica gel was scraped from the chromatoplate, extracted with 50 ml of acetonitrile and analyzed by HPLC.

2.3 In water

Each benzanilide (I: X = Me; Y = 2'-MeO, 3'-MeO, 3'-i-PrO,4'-MeO or H) was stirred in 100 ml of water for one day and filtered to prepare the saturated solution. Thirty ml of the solution were placed in a 30 ml flask, covered with thin film of Krewrap, exposed to sunlight for a specified period, and analyzed by HPLC.

3. Analysis

It is quite difficult to detect *o*-toluamide by gas chromatography or to convert it quantitatively to a derivative which is analyzable. This difficulty was shared by other 2-substituted benzamides studied. Therefore, high performance liquid chromatography (HPLC) was adopted for analysis of initial and degraded Journal of Pesticide Science 9 (3), August 1984

	Degraded benzanilide and produced photoproducts (%)								
Benzanilide	Benzar	Benzanilide		Benzamide		Benzoic acid		CO ₂ (mg)	
	5 (days)	10	5	10	5	10	5	10	
3'-MeO-2-MeO	50.9	61.2	8.5	10.0	1.3	7.9	0.7	1.9	
3'-MeO-2-Me	34.8	54.9	12.8	16.7	0.2	2.2	1.3	2.3	
3'-MeO-2-H	42.8	52.7	12.6	17.2	9.8	11.0	1.3	2.4	
3'-MeO-2-Cl	29.0	51.6	15.1	19.6	11.0	6.6	1.2	2.6	
3'-MeO-2-CF ₃	38.4	46.4	8.9	15.6	1.1	1.1	1.2	2.1	
3′-i-PrO-2-Me (Mepronil)	35.6	65.2	7.7	11.7	0.1	1.0	0.7	2.4	

Table 2 Photodegradation of various benzanilides in the presence of xanthone.

samples using weak ultravoilet adsorption at 254 nm as detection measure. The retention time of 2-substituted benzoic acids was too short under the present reverse phase HPLC conditions. Thus they were analyzed as the methyl esters obtained by reaction with diazomethane. The conditions of HPLC using a Waters model system 45 were as follows. Column system: radial compression system RCM-100 (Waters); column: radial pak C-18 ϕ 5 mm (Waters); detector: HPLC model 440, 254 nm at 0.02 AUFS; mobile phase: acetonitrile/water (55/45); flow rate: 1.3 ml/min; and recorder: UNICORDER U-228 (Nihon Denshi Kagaku) with scanning speed of 1 cm/ min. The retention time of each compound is shown in Table 1. Carbon dioxide evolved was measured by the weight increment of Ascarite.

RESULTS AND DISCUSSION

1. Benzamide Production on Silica Gel 1.1 With sunlight

Benzamide, benzoic acid and CO_2 as well as remaining benzanilide were determined after 5 and 10 days exposure to sunlight of mepronil and five 3'-methoxy-2-substituted benzanilides adsorbed on silica gel (Table 2). Degradation of 2-MeO, 2-Me, 2-H, and 2-CF₈ compounds proceeded rapidly during the initial 5 days and slowed down afterwards. For example, degradation of 2-MeO compound was 50.9% after 5 days, but 61.2% even after 10 days. On the other hand, 2-Cl compound and mepronil degraded at a steadier rate: 29.0 and 35.6% after 5 days and 51.6 and 65.2% after 10 days respectively. Benzamide formation was 16-20% after 10 days for 2-Me, 2-H, 2-Cl and 2-CF₃ compounds, and 10% for 2-MeO com-When 3'-MeO-2-Me and 3'-i-PrO-2pound. Me (mepronil) compounds are compared, the former gave less degradation and more benzamide formation. This means that substituent on aniline moiety also affect the reaction Benzoic acid formation on day 10 course. when compared with that on day 5 was varied: increased for 2-MeO, 2-Me compounds and mepronil, kept constant for 2-H, 2-CF₃ and decreased for 2-Cl compound. The results indicate that certain substituted benzoic acids when formed will be lost during exposure, while benzamide formed stayed on silica gel during exposure. Combined amount of benzamide and benzoic acid products was 10-26% after 5 days and 18-28% after 10 days. The rest was unidentified products and CO₂. The amount of CO₂ increased with the lapse of time and was similar to different compounds: 2.6 mg of CO₂ correspond to 5.1×10^{-4} mol, which were obtained from 3.3×10^{-5} mol of 2-Cl compound. Thus photoreaction which produces o-toluamide from mepronil is quite general for other benzamides. Although substituent effect was observed, it was difficult to quantify the effect from this experiment.

1.2 With ultraviolet ray

Photodegradation of benzanilide compounds and formation of benzamides were examined under more controlled conditions for analyzing substituent effect on degradation. Each benzanilide (I: X=Me, MeO, Cl, NO₂, or H; Y=3'-MeO or 3'-i-PrO) was irradiated with 422

ultraviolet ray on silica gel chromatoplate for 20 hr. Combined amount of benzanilide remained and benzamide formed was over 80%except the case of $2-NO_2$ compound (43.7%). In the following description, the first figures in percent represent the benzanilide remained and the second figures represent the benzamide produced. Figures of six compounds were as follows: 3'-MeO-2-MeO (83.6; 3.4%), 3'-MeO-2-Me (98.0; 2.1%), 3'-MeO-2-H (76.9; 3.0%), 3'-MeO-2-Cl (78.3; 7.8%), 3'-MeO-2-NO₂ (41.9; 1.8%), and 3'-i-PrO-2-Me (97.7; 3.1%). Particularly, in the case of mepronil (3'-i-PrO-2-Me) and 3'-MeO-2-Me compound, o-toluamide was almost the sole photoproduct. Although regression analysis on the relationship between the degradation rate and various substituent constants was attempted, the number of cases was not enough to justify the establishment of the relation. However, some insight was obtained from the nature of the substituents. If the degradation rate follows the order of the electron drawing ability of the o-substituents, it should be NO₂ (σ =0.78)>Cl (0.23)>H (0)> Me (-0.17) > MeO (-0.27). On the other hand, if the rate follows the bulkiness of the substituents, it should be NO₂ (Es = -2.52) >Me (-1.24) > Cl (-0.97) > MeO (-0.55) > H (0). The actual degradation rate was in order of $X = NO_2 > H \ge Cl > MeO > (mepronil) \ge Me.$

Therefore, it is suggested that the rate of degradation is accelerated by the electron drawing ability of the substituent, but the bulkiness of the substituent slows down the rate. The overall effect of the electronic and steric effect is reflected on the result we observed.⁵⁾

There seem to be two ways of cleavage of amide linkage (Fig. 1). In the previous paper,³⁾ it was reported that [aniline-U-¹⁴C]mepronil gave more radioactivity corresponding to highly polar products and volatiles than [carbonyl-¹⁴C]mepronil. Also, major radioactive products were *o*-toluic acid and *o*toluamide from the latter. In the present experiment, benzamide formation was found to be accompanied by CO₂ formation. The results are understandable when we postulate that initially photo-oxidation occurs on the aniline ring, which triggers the cleavage of bond between nitrogen and ring carbon, and the ring Table 3 Changes of benzanilides and isoindolines in water exposed to sunlight.

Benzanilides	Benzanilides and isoindolines (%)					
T ! J. 1'	(weeks)					
Isoindolines	1	2	´ 4	8		
2'-MeO-2-Me	73.2	56.3	22.2	19.5		
2'-MeO	13.4	30.9	33.8	27.7		
3'-MeO-2-Me	91.0	81.9	65.4	50.3		
3'-MeO	10.0	17.1	29.6	43.7		
4'-MeO-2-Me	61.8	56.2	13.0	2.2		
4'-MeO	9.1	24.8	21.9	30.0		
H-2-Me	96.9	91.2	76.4	60.1		
Н	3.4	3.5	10.8	15.1		
Mepronil	92.8	83.5	65.8	32.4		
3'-i-PrO	4.0	14.2	29.3	25.9		



Fig. 1 Formations of benzamides and isoindoline compounds.

here indicates benzene or partially hydrogenated benzene ring.

is ruptured eventually to CO₂, while cleavage also occurs between amide carbonyl and nitrogen to give benzoic acid and aniline compounds, the latter polymerizing and staying at the origin when chromatographed on thinlayer plate.

2. Isoindoline Production in Water

Each benzanilide (mepronil or I: X=Me, Y=2'-MeO, 3'-MeO, 4'-MeO or H) was exposed to sunlight in water for 8 weeks. As shown in Table 3, the photodegradation of compounds was in the order of 4'-MeO>2'-MeO>mepronil>3'-MeO>H. Combined amount of benzanilide remained and isoindoline produced was over 80% except 4'-MeO compound (71%) after 2 weeks, and it is generally said that isoindoline is the major photoproduct under this Degradation was faster when condition. electrodonating methoxy group locates at 4 and 2 positions than 3 position or no substitution. Isoindoline products increase with the lapse of time except the case of isoindoline from mepronil which decreased after 8 weeks. This may be due to the instability of 3'-isopropoxy Thus, formation of isoindoline from group. benzanilide is shown to be a general reaction in water. As reported in the previous paper, 2-methyl group is first hydroxylated, then further oxidized and cyclized to give isoindoline products (Fig. 1).

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要 約

ベンズアニリド類の光分解におけるベンズアミ ドとイソインドリン化合物の生成

弓田隆司,嶋崎 功,宮本 徹,山本 出 メプロニルの薄層クロマト板上での太陽光による分解 では、o-toluamide が、また水溶液中における紫外光線 による分解では、1-hydroxy-3-oxo-2-(3'-isopropoxyphenyl)isoindoline が主要生成物である。これら両者の 生成を、他のベンズアニリドにおいて検討した結果、一 般的な光反応であることを見いだした。また、3'-メトキ シ-2-置換ベンズアニリド類の紫外光線による薄層クロ マト板上での分解では、分解速度とオルト置換基効果と の間に相関性を見いだした。