The Formation of 2-Chlorobenzamide upon Hydrolysis of the Benzoylphenylurea Insecticide 1-(2-Chlorobenzoyl)-3-(4-chlorophenyl) Urea in Different Water Systems

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It has been reported that 1-(2-chlorobenzoyl)-3-(4-chlorophenyl) urea (CCU), an insect growth regulator, has no measurable toxicity to nontarget organisms and is essentially harmless to humans. However, one of its degradation products, 2-chlorobenzamide (CBA), is suspected of being a carcinogen. Therefore, the maximum concentration of CBA formed and the dynamics of its formation need to be given careful attention after CCU is used in the field. This paper describes the degradation of CCU to form CBA in three different water systems (distilled water, spring water, and simulated seawater) and the effects of temperature on the dynamics of CBA formation. The results indicate that the maximum level of CBA concentration is different in the different systems (highest in spring water) and that the temperature has a significant impact on the process (higher temperature leads to higher and earlier peak of CBA concentration). The maximum concentration of CBA after application of CCU was approximately 3.8% of the initial concentration of CCU at 35 °C in distilled water, and 2.4% in spring water at 25 °C.

1. INTRODUCTION

Attempts to resolve pest problems through chemical control have resulted in the discovery of highly selective insecticides, such as the benzoylphenylureas (BPUs). Diflubenzuron is the first known insecticide of the BPUs and has been widely used in Europe and the U.S. since the 1970s (*1–4*). The persistence and fate of diflubenzuron in and on plants and in soils have been reported (*5–8*). The metabolism of diflubenzuron has been reviewed by Ivie (*9*) and Schooley and Quistad (*10*). CCU is another insecticide of the BPUs that was developed after diflubenzuron and has been widely used in China since 1976. Previous papers indicate that CCU provides good control of the pine moths in forestry, army worms in wheat and corn, and cabbage caterpillars in vegetables of China (*11–14*), as well as *Heliothis armigera*, *Ostrinia furnacalis*, *Pseudaletta separata (walker)*, *Dendrolimus tabulaeformis*, *Hyphantria cunea*, *Pieris rapae L.*, and golden flower worms (*13, 15*).

CCU is effective as both a stomach and contact poison through inhibition of chitin synthesis and interference with cuticle formation. Further studies have demonstrated that CCU is a compound of low mammalian toxicity, as its acute oral LD_{50} values for rats and mice are greater than 10000 mg/kg (*16*). It is not toxic to birds, fishes, and bees, and it has no teratogenesic or mutagenesic effects (*17, 18*). The behavior of CCU in plants, water, soil, air, and fish has been described, with 2-chlorobenzamide (CBA) always being identified as one

of the chief degradation products (*16, 19–31*). Both Ames mutagenesis and DNA adduct experiments with CBA all showed positive results, which suggest that CBA might be a potential carcinogen (*32*). The degree of formation of CBA from CCU and the timing of the occurrence of the peak concentration of CBA might determine whether CCU can be used widely in agriculture. Based on these concerns, we investigated the relationship between CCU and CBA in three different water systems (distilled water, spring water, and simulated seawater) in order to supply valuable data that can be used to evaluate the environmental safety of CCU.

2. MATERIALS AND METHODS

2.1. Instruments and Chemicals. A high-performance liquid chromatograph (HPLC), Shimadzu model LC-6A (Japan), with a Shimadzu SPD-6AV UV−VIS spectrophotometric detector and a 250 × 4.6 mm ZORBAX-ODS reversed-phase column, was used for all quantitative analysis.

CBA was obtained from the Research Centre of Eco-Environmental Sciences, Chinese Academy of Sciences, Beijing, China. CCU was supplied by Anyang Forestry Chemical Factory.

2.2. Verification of the Purity of CCU and CBA. After being recrystallized three times with anhydrous ethanol, CCU showed no impurity peak on the HPLC, and its infrared spectrum was identical with that cited in the literature (*33*).

CBA was analyzed on the HPLC, and its infrared spectrum was obtained. The infrared spectrum conformed to the standard spectra for CBA (*34*). The results of the HPLC analysis showed that CBA had no impurity peak.

2.3. Preparation of the Stock Solutions. CCU (500 mg) was weighed accurately to ±0.1 mg and added to approxi-

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mately 100 mL of methanol under ultrasonication. The volume was made up to 100 mL with methanol and then stored in the refrigerator for use. The CBA stock solution was prepared in the same manner using 493 ± 0.1 mg of CBA.

2.4. Analysis and Standard Curves. *2.4.1. CCU Standard Curve and Chromatography Conditions.* A series of solutions was prepared with concentrations of 0.5, 1, 5, 10, 20, 30, and 50 ppm by diluting with a 500 ppm CCU stock solution with water. The solution concentrations were determined by HPLC using the following conditions:

HPLC column:	250 × 4.6 mm, ZORBAX-C18
mobile phase:	$CH_3OH:H_2O = 80:20$ (v/v)
detector:	SPD-6AV UV−VIS spectrophotometric detector
flow rate:	1 mL/min
wavelength:	206 nm
temp. of column:	32 °C
input sample volume:	5 μL

Plotting the concentration of CCU on the *y* axis and the peak area of CCU on the *x* axis, a straight line was obtained, which demonstrates a very strong linear relationship (regression correlation coefficient = 0.9998) from 0.5 to 50 ppm. The relationship between the CCU concentration and the peak area can be described by the equation $C = 5.33 \times 10^{-5}A + 0.9437$, where A = peak area of CCU and C = CCU concentration.

2.4.2. CBA Standard Curve. The procedure for obtaining the CBA standard curve was the same as that for CCU, but concentrations of 0.986, 4.93, 9.86, 14.79, 19.72, and 29.58 ppm were used. The mobile phase for HPLC analysis was methanol/water (40:60 v/v). A strong linear relationship between CBA concentration and peak area was observed. The relationship between the CBA concentration and the peak area can be described by the equation $C = 4.781 \times 10^{-5}A + 0.448$, where A and C are defined as above, but for CBA.

2.5 Hydrolysis of CCU. *2.5.1. Recovery of CBA and CCU.* Twice-distilled water was fortified to concentrations of 0.1, 0.5, and 1 ppm with CCU stock solution (500 ppm). To determine the diluting concentrations of CCU, duplicate 10 mL aliquots were removed from each concentration and extracted with 3×10 mL aliquots of dichloromethane (freshly distilled). The extracted solutions were combined and dried over anhydrous Na_2SO_4. The combined aliquots were evaporated to near dryness in a rotatory film vacuum evaporator, and the residues were then dissolved in 1 mL of anhydrous methanol (freshly distilled) and analyzed by HPLC for CCU using conditions similar to those described in section 2.4.1 except for the following changes:

mobile phase:	methanol/water = 70:30 (v/v)
flow rate:	0.6 mL/min

The process of CBA recovery was the same as above using the HPLC conditions described in section 2.4.2.

2.5.2. Hydrolysis in Distilled Water Systems. Three replicate samples of 300 mL of distilled water were fortified by adding 5 mL of CCU stock solution dropwise under ultrasonication. These samples were then placed in thermostatically controlled chambers maintained at 25 °C in the dark. Samples were drawn at 5-day intervals up to a maximum of 55 days and extracted and analyzed for CCU and CBA as described in section 2.5.1.

2.5.3. Hydrolysis in Simulated Seawater Systems. Seawater has a very variable composition, and it is not conveniently obtained. Therefore, to study the hydrolysis of CBA in seawater, simulated seawater (*35*), which is easily made and has a composition very close to that of natural seawater, was used (Table 1). Solutions of CCU in seawater were made to the same concentrations as in distilled water, and they were sampled at the same intervals, extracted, and analyzed for CCU and

Table 1. Composition of Simulated Sea Water

compound[a]	quantity[b]	unit
NaCl	23.926	g
Na_2SO_4	4.0013	g
KCl	0.6772	g
$NaHCO_3$	0.1962	g
NaF	0.0034	g
H_3BO_3	0.026	g
KBr	0.097	g
$MgCl_2$ (1.0 mol/L)	53.28	mL
$CaCl_2$ (1.0 mol/L)	10.33	mL
$SrCl_2$ (1.0 mol/L)	0.90	mL

[a] Composition from Dai et al. (*35*) [b] Add components to distilled water and make up to 1000 g.

Table 2. Recovery of CCU and CBA from Distilled Water

CCU	fortified conc. (ppm)	0.1	0.5	1
	recovery (%)	92.3	94.5	91.5
CBA	fortified conc. (ppm)	0.493	0.799	0.986
	recovery (%)	88.8	93.2	96.8

CBA using the same method as for the distilled water system, described in section 2.5.2.

2.5.4. Hydrolysis in Spring Water. Natural spring water (1000 mL) was taken from a natural Baiquan spring located 2 km north of Huixian, Henan Province, China. It was treated with active carbon and then filtered with two layer filters. The filtered water was stored for use. Solutions of CCU in spring water were made to the same concentrations as in distilled water, and they were sampled at the same intervals, extracted, and analyzed for CCU and CBA using the same method as for the distilled water system, described in section 2.5.2.

2.5.5. The Effects of Temperature on Hydrolysis of CCU to CBA. An experiment was designed to investigate the effects of temperature on the relationship between the concentrations of CCU and its hydrolysis product CBA in distilled water systems. Solutions of CCU were made for three separate distilled water systems to the same concentrations, and they were sampled at the set intervals, extracted, and analyzed for CCU and CBA using the same method as for the distilled water system, described in section 2.5.2. The temperatures of the three systems were maintained at 25, 35, and 45 °C.

3. RESULTS AND DISCUSSION

3.1. Recoveries of CCU and CBA from Water. The data for the recovery of CCU from water through extraction shown in Table 2 demonstrate that the recovery of CCU is independent of the fortified concentration and ranges between 91 and 95%. The recovery of CBA from water increased slightly with the increase in the fortified concentration of CBA, but was above 88% in all cases.

3.2. Hydrolysis of CCU to CBA. The variations in CBA following the hydrolysis of CCU applied to distilled water, simulated seawater, and spring water at 25 °C were investigated, and the results are exhibited in Figures 1−3. From Figure 1, we can see that CCU hydrolyzed in distilled water with a $t_{1/2}$ of 8 days, which is similar to the 7 days reported for diflubenzuron, a compound of similar structure (*36*). The maximum concentration of CBA formed was about 1.6% of the initial CCU molar concentration, also similar to the concentration of DFBA (difluorobenzamide) found for diflubenzuron (*36*), and this maximum concentration occurred on day 22 after application of CCU. CCU degraded quickly in simulated seawater, but the maximum concentration of CBA was observed on day 40 (Figure 2), significantly later than in distilled water. Baiquan spring water is very similar to surface water and was selected to represent surface water in the
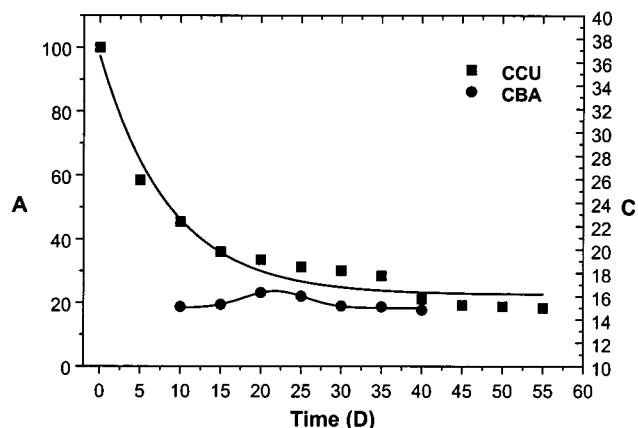
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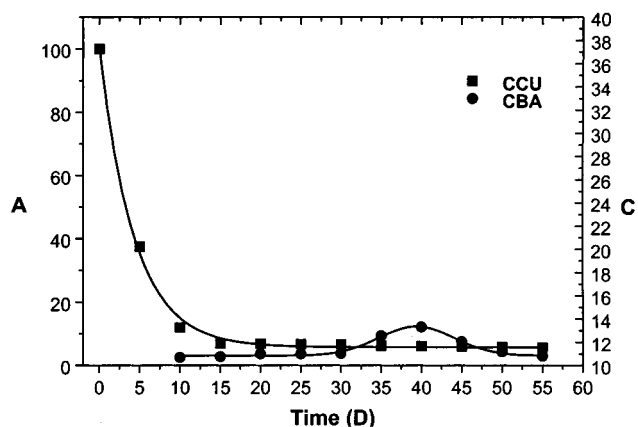**Figure 1.** Relationship between CCU and CBA in distilled water at 25 °C.

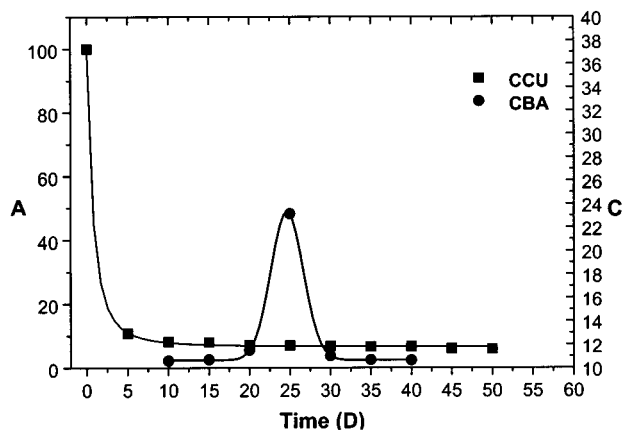**Figure 2.** Relationship between CCU and CBA in simulated seawater at 25 °C.

Figure 3. Relationship between CCU and CBA in Baiquan spring water at 25 °C. (A) Ratio of CCU concentration to its initial concentration × 100. (C) Ratio of CBA concentration to the initial concentration of CCU × 1000.

Figure 4. Relationship between CCU and CBA at 25 °C.

Figure 5. Relationship between CCU and CBA at 35 °C.

Figure 6. Relationship between CCU and CBA at 45 °C. (A) Ratio of CCU concentration to its initial concentration × 100. (C) Ratio of CBA concentration to the initial concentration of CCU × 1000.

investigation of CCU degradation. CCU hydrolyzed faster in this system than in distilled water or simulated seawater, showing 90% CCU degradation at day 10. The maximum concentration of CBA was observed on day 25, and this maximum concentration reached approximately 2.4% of the initial molar concentration of CCU (Figure 3), higher than in the other two systems. The results suggest that the hydrolysis of CCU might be catalyzed by unknown substances in spring water.

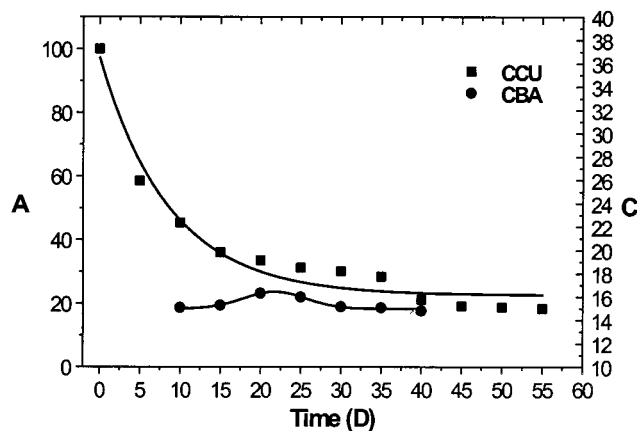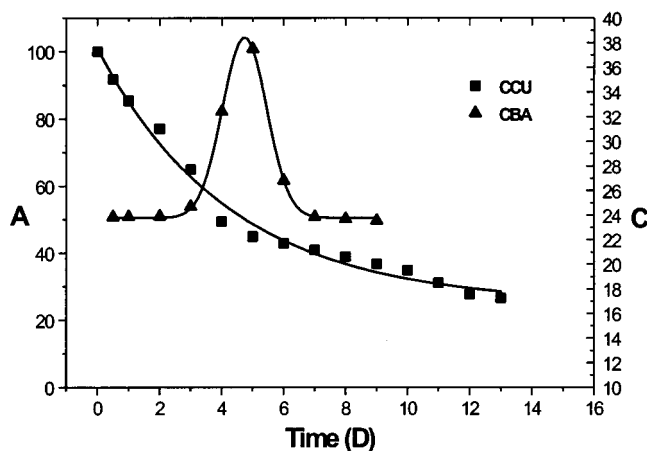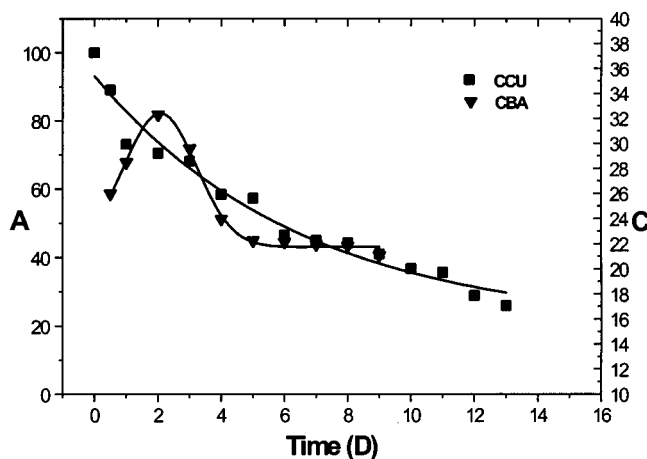**3.3. The Effect of Temperature on the Hydrolysis of CCU and the Relative CBA Concentration.** The degradation of CCU to CBA in distilled water in response to different temperatures is shown in Figures 4−6. The results show that temperature plays an important role in the hydrolysis of CCU and in the formation of CBA. Degradation of CCU becomes faster with increasing temperature, ($t_{1/2}$ = 8, 5, and 5 days at 25, 35, and 45 °C, respectively), and the peak of the CBA concentration is observed earlier (day 22 at 25 °C, day 5 at 35 °C, and day 2 at 45 °C). Under these conditions, the maximum concentration of CBA was found to be between 1.6 and 3.8% of the initial concentration of CCU.
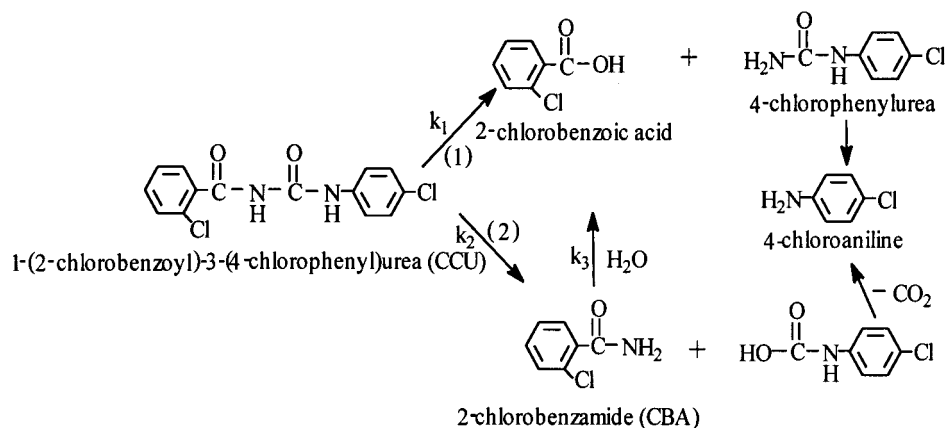
Figure 7. Proposed hydrolytic pathway of CCU.

3.4. Kinetic Analysis of CBA Formation. CCU hydrolyzes mainly through two different processes, as shown in Figure 7 (*25*), which is similar to the hydrolysis pathway proposed for the related diflubenzuron (*36*). Pathway 1, in which CCU is hydrolyzed to 2-chlorobenzoic acid and 4-chlorobenzylurea, is the main hydrolytic pathway, but its rate constant k_1 is unknown and cannot be determined from these studies because the concentration of either degradation product was not determined. Pathway 2 is more complex, and the rate of this pathway is also not known. We do not have enough information for a calculation, but we can present a theoretical analysis of the kinetics of the accumulation and decline of CBA. The rate constant for the hydrolysis of CCU to CBA (k_2 in pathway 2) is small, and also the rate constant k_3 for the formation CBA hydrolyzing to 2-chlorobenzoic acid is very low (*37*), resulting in a CBA concentration that can be observed over several days. The dynamics of the formation of the maximum concentration can be followed according to pathway 2.

If the initial concentration of CCU is set to a, the initial concentration of CBA is set to zero, and the concentrations of CCU and CBA at time t are set to x and y, respectively, then the following equations can be suggested:

$$-\frac{dx}{dt} = k_1 x + k_2 x \tag{1}$$

$$\frac{dy}{dt} = k_2 x - k_3 y \tag{2}$$

Because eq 1 has the form of a simple first-order reaction, $\ln a/x = (k_1 + k_2)t$, which can be rearranged to $x = ae^{-(k_1+k_2)t}$. Combining eqs 1 and 2, we can derive the following equation:

$$\frac{dy}{dt} = k_2 a e^{-(k_1+k_2)t} - k_3 y$$

This equation has the form of a simple linear partial equation, namely, $dy/dx + Py = Q$; therefore, we can solve for y.

$$y = \frac{k_2 a}{k_3 - (k_1 + k_2)}[e^{-(k_1+k_2)t} - e^{-k_3 t}]$$

The time of the formation of the maximum CBA concentration t_m can be calculated as in the equation.

$$t_m = \frac{\ln k_3 - \ln(k_1 + k_2)}{k_3 - (k_1 + k_2)}$$

The maximum CBA concentration y_m can also be calculated via

$$y_m = \frac{k_2}{k_3} a \left(\frac{k_1 + k_2}{k_3}\right)^{(k_1+k_2)/[k_3-(k_1+k_2)]}$$

4. CONCLUSION

When CCU degrades in different water systems, temperature plays an important role in the quantity of CBA formed and the appearance of the peak concentration. With an increase in temperature, the peak in the CBA concentration is observed earlier than at lower temperatures. The maximum concentration of CBA was the highest in spring water and was much lower in distilled water and simulated seawater. The effect of pH on the degree of formation of CBA is also likely to be important, as it is for diflubenzuron (*36*), but it was not investigated in this paper.

The hydrolytic rate of CCU is different in different water systems, being faster in spring water and in simulated water and slower in distilled water. Perhaps some ion or microorganism catalyzes the degradation of CCU in the spring water and seawater, but this is speculation and needs to be investigated. It is theorized that the main degradation pathway for CCU produces 4-chlorophenylurea and 2-chlorobenzoic acid, but the pathway by which CCU produces CBA is an important pathway because of the potential health concerns from CBA. Although its maximum concentration is relatively low, CBA should be given more attention because it hydrolyzes slowly and might be present over long periods of time.

LITERATURE CITED

(1) Hajjar, N. P.; Casida, J. E. Insecticidal benzoylphenyl ureas: structure–activity relationships as chitin synthesis inhibitors. *Science* **1978**, *200*, 1499.

(2) Mulder, R.; Gijswijt, M. J. The laboratory evaluation of promising new insecticides which interfere with cuticle deposition. *Pestic. Sci.* **1973**, *4*, 737.

(3) Post, L. C.; deJong, B. J.; Vincent, W. R. 1-(2,6-Disubstituted benzoyl)-3-phenylurea insecticides. Inhibitors of chitin synthesis. *Pestic. Biochem. Physiol.* **1974**, *4*, 473.

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(4) Veloop, A.; Ferrell, C. D. Benzoylphenyl ureas—a new group of larvicides interfering with chitin deposition. *Am. Chem. Soc. Symp. Ser.* **1977**, *37*, 237−270.

(5) Bull, D. L.; Ivie, G. W. Fate of diflubenzuron in cotton, soil, and rotational crops. *J. Agric. Food Chem.* **1978**, *26*, 515−520.

(6) Metcalf, R. L.; Lu, P. Y.; Bowlus, S. Degradation and environmental fate of 1-(2,6-difluorobenzoyl)-3-(4-chlorophenyl) urea. *J. Agric. Food Chem.* **1975**, *23*, 359−364.

(7) Schaefer, C. H.; Dupras, E. F. Residues of diflubenzuron-[1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl) urea] in pasture soil, vegetation, and water following aerial application. *J. Agric. Food Chem.* **1977**, *25*, 1026.

(8) Austin, D. J.; Hall, K. J. A method pf analysis for the determination of binapacryl, bupirimate and diflubenzuron on apple foliage and fruit, and its application to persistence studies. *Pestic. Sci.* **1981**, *12* (5), 495−502.

(9) Ivie, G. W. In *Fate of Pesticides in Large Animals*; Ivie, G. W., Dorough, H. W., Eds.; Academic Press: New York, 1977.

(10) Schooley, D. A.; Quistad, G. B. Metabolism of insect growth regulators in quatic organisms. *ACS Symp. Ser.* **1979**, *10*, 161.

(11) Chen, K.; Gu, D.; Ji, Y.; Lu, Zh. Inhibitors of chitin synthesis enzymes: CCU and PH6038. *Nongyao (China)* **1980**, *19* (1), 44−45.

(12) Li, M.; Li, B. Study on the processing methods of organophosphorus powders. *Nongyao (China)* **1981**, *20* (2), 1−7.

(13) Chen, K.; Lu, Zh.; Lu, D. A new insecticide of 1-(2-chlorobenzoyl)-3-(4-chlorophenyl) urea. *Nongyao (China)* **1984**, *23* (2), 21.

(14) Lu, Zh.; Chen, K.; Lu, D.; Gu, D. Spectral and physical characters of 1-(2-chlorobenzoyl)-3-(4-chlorophenyl) urea. *Nongyao (China)* **1981**, *20* (6), 23.

(15) Xie, D.; Ling, R.; Li, J.; Liu, B.; Tan, Y. Preliminary report of potent experiment to pieris rapae L. of 1-(2-chorobenzoyl)-3-(4-chorophenyl) urea. *ACTA of Guangxi Academy of Sciences (China)* **1986**, *2* (2), 73−79.

(16) Mo, H.; An, F.; Yang, K.; Bi, W.; Deng, W. Residue and persistence of insecticide 1-(2-chorobenzoyl)-3-(4-chorophenyl) urea in Chinese cabbage and soils in Northern China. *J. Environ. Sci. (China)* **1992**, *4* (4), 24.

(17) Sun, J.; Qian, Z.; Sun, W.; Jiao, S. Safety assay of 1-(2-chorobenzoyl)-3-(4-chorophenyl) urea on bees and chihuo zao yang. *Nongyao (China)* **1982**, *21*(1), 60.

(18) Lu, D.; Lu, Zh.; Chen, K. General report of toxic assay of 1-(2-chorobenzoyl)-3-(4-chorophenyl) urea. *Nongyao (China)* **1983**, *22* (5), 24.

(19) An, F.; Mo, H.; Bi, W.; Deng, W. *Proceedings on the studies on the environmental behavior and eco-toxicology of toxic organics*; Xu, X., Ed.; China Science and Technology Press: Beijing, China, 1990.

(20) Zhou, Z.; Xu, Z.; Weng, C.; Mo, H. Study on the residue of 1-(2-chorobenzoyl)-3-(4-chorophenyl) urea in Chinese cabbage and soil in the southern China and its distribution in laboratorial microcosm. *J. Environ. Sci. (China)* **1992**, *4* (4), 30.

(21) Jobelius, M. H.; Zhang, Y.; Xu, Y.; Chen, Z. *Proceedings on the studies on the environmental behavior and eco-toxicology of toxic organics*; Xu, X., Ed.; China Science and Technology Press: Beijing, China, 1990; p 53.

(22) Xu, Y.; Xu, L.; Zhang, Y. *Proceedings on the studies on the environmental behavior and eco-toxicology of toxic organics*; Xu, X., Ed.; China Science and Technology Press: Beijing, China, 1990; p 58.

(23) Yang, D.; Yang, S.; Lei, Z.; Yang, K.; Mo, H.; Dai, G. *Symposium on environmental behavior and ecotoxicity of organic compounds*; Xu, X., Ed.; China Science and Technology Press: Beijing, China, 1990.

(24) Yang, K. Ph. D. dissertation. Research Centre for Eco-Environmental Sciences, Chinese Academy of Sciences, Beijing, China, 1991.

(25) Yang, K.; Mo, H.; Xu, X.; Dai, G. Hydrolysis of 1-(2-chorobenzoyl)-3-(4-chorophenyl) urea in aquatic systems. *J. Environ. Sci. (China)* **1992**, *4* (4), 10.

(26) Shi, G. Study on the degradation and transformation of 1-(2-chorobenzoyl)-3-(4-chorophenyl) urea insecticide by soil microorganisms under needles and broad leaf forest. *J. Environ. Sci. (China)* **1992**, *4* (4), 37.

(27) Liu, G.; Jin, Z.; Xu, X. Photoreaction of 1-(2-chorobenzoyl)-3-(4-chorophenyl) urea in simulated atmosphere. *J. Environ. Sci. (China)* **1992**, *4* (4), 52.

(28) Mo, H.; An, F.; Yang, K.; Zhang, L.; Xu, X.; Yang, D.; Yang, S.; Lei, Z. *Environ. Hydraulics*; Lee, J. H. W., Cheng, Y. K., Eds.; Balakema, A. A.: Rotterdam, The Netherlands, 1991; p 1355.

(29) Mo, H.; An, F.; Zhou, Z.; Xu, Z.; Weng, C.; Bi, W.; Deng, W. Study on residues and persistence of insecticide 1-(2-chorobenzoyl)-3-(4-chorophenyl) urea (CCU) in Chinese cabbage and soil. *Huanjing Kexue (China)* **1991**, *12* (4), 73−78.

(30) Mo, H.; Zhang, L.; Xu, X. Review of the environmental behavior of insecticide 1-(2-chorobenzoyl)-3-(4-chorophenyl) urea. *J. Environ. Sci. (China)* **1992**, *4* (4), 81.

(31) Zhang, Y.; Xu, Y.; Xu, L.; Chen, Z. Degradation of chlorobenzuron in water and metabolism in fish. *J. Environ. Sci. (China)* **1992**, *4* (4), 46.

(32) Liu, S.; Jiang, X.; Liu, G.; Xu, X. Investigation of DNA-2-chlorobenzamide adduct. *Environ. Sci. (China)*, **1997**, *16* (4), 316.

(33) Liu, G. Ph. D. dissertation. Research Centre for Eco-Environmental Sciences, Chinese Academy of Sciences, Beijing, China, 1990.

(34) Standard Infrared Grating Spectra; Sadtler Research Laboratories, Inc., U.S.A., 1974, Vol. 33−34, No. 32167k.

(35) Dai, Sh.; Chen, F.; Wang, Sh. In *Huanjing Huaxue*; Dai, Sh., Chen, F., Wang, Sh., Eds.; High Education Press: Beijing, China, 1987; p 161.

(36) Ivie, G. W.; Bull, D. L.; Veech, J. A. Fate of diflubenzuron in water. *J. Agric. Food Chem.* **1980**, *28*, 330−337.

(37) Zhou, Q.; Lu, W.; Liu, G.; Xue, X. Study on the hydrolysis of 2-chlorobenzamide. *J. Agric. Food Chem.* **2000**, *48* (6), 2572−2575.