Hydrolysis Kinetics of Fenthion and Its Metabolites in Buffered Aqueous Media

Jiping Huang and Scott A. Mabury*

Department of Chemistry, University of Toronto, Toronto, Ontario M5S 3H6, Canada

This study investigates the hydrolysis kinetics of fenthion and its five oxidation metabolites in pH 7 and pH 9 buffered aqueous media at 25, 50, and 65 °C. Five metabolites and three hydrolysis products were synthesized and purified. The reactant and the corresponding hydrolysis products were determined by HPLC. Rate constant and half-life studies revealed that fenthion and its metabolites were relatively stable in neutral media, and their stability decreased as pH increased. The half-lives at 25 °C ranged from 59.0 days for fenthion to 16.5 days for fenoxon sulfone at pH 7, and from 55.5 days for fenthion to 9.50 days for fenoxon sulfone at pH 9; half-lives were greatly reduced at elevated temperatures. The activation energy (E_a) was found to range from 16.7 to 22.1 kcal/mol for the compounds investigated. The phenol hydrolysis product of fenthion and fenoxon, 3-methyl-4-methylthiophenol was not stable in pH 7 and pH 9 buffered solutions at 50 °C, whereas 3-methyl-4-methylsulfonylphenol and 3-methyl-4-methylsulfinylphenol were relatively stable under the same conditions. At pH 9, the primary hydrolysis mechanisms of fenthion and its oxidation metabolites were combination of hydroxide ion and neutral water molecule attacking on the P atom to form corresponding phenol derivatives. Under neutral conditions, the primary hydrolysis mechanisms of fenthion and its oxidation metabolites were assumed to be the combination of water molecule attacking on the P atom to form phenol derivatives and on the C atom to yield dealkylation products.

Keywords: *Fenthion; metabolites; hydrolysis; kinetics; half-life*

INTRODUCTION

Organophosphorus insecticides are widely used in agriculture and animal production for the control of various insects. These compounds generally have higher acute toxicity than chlorinated insecticides, which is due to the inhibition of the enzyme cholinesterase, an essential component of the animal nervous system (Aly and Badaway, 1982). The persistence of organophosphorus insecticides in aquatic environments is affected by several factors, such as oxidation, photolysis (Ohkawa et al., 1974), and biological degradation (Ruzicka et al., 1967). Chemical hydrolysis of organophosphorus insecticides was reported to play an important role in the persistence of these compounds in the environment (Cowart et al., 1971). In addition to the aquatic environment, rainfall, atmospheric water vapor, and soil moisture all provide ample opportunity for hydrolysis.

Fenthion (*O*,*O*-dimethyl *O*-[4-(methylthio)-*m*-tolyl] phosphorothioate (**I**) (Figure 1) is used as a contact and stomach insecticide in the control of fruit flies in many crops (Cabras et al., 1991). Once used extensively, fenthion was classified by the U.S. EPA as a Restricted Use Pesticide (RUP) due to its toxicity (Kamrin, 1997). Residual levels of fenthion have been reported in various environmental matrices (Wang et al., 1987). Five oxidation metabolites of fenthion have been isolated in animals and plants and include fenthion sulfoxide (**II**), fenthion sulfone (**III**), fenoxon (**IV**), fenoxon sulfoxide (**V**), and fenoxon sulfone (**VI**) (Figure 1) (Cabras et al., 1993). The metabolites showed higher toxicity than the parent compounds: the lethal dose (LD_{50}) was 220 mg/kg for **I**, 125 mg/kg for **II**−**IV**, 50 mg/kg for V, and 30 mg/kg for **VI**. The sulfoxide (**II**) and sulfone (**III**) were observed as fenthion photolysis products on orange fruit surfaces (Minelli et al., 1996). Photoinduced oxidation of sulfur to the sulfoxide and sulfone has been commonly observed in water or simulated natural waters; examples include molinate and thiobencarb (Draper and Crosby, 1984) and albendazole (Weerasinghe et al., 1992). Oxidation of the sulfur in phosphorothioates has also been observed in field water (e.g., fenitrothion to fenitrooxon), although the oxon derivative is generally unstable (Lacorte and Barcelo, 1994). Since hydrolysis is one of the principal detoxification mechanisms for organophosphorus insecticides, hydrolysis of **I**−**VI** leads to compounds of low toxicity (FAO/WAO, 1971). The

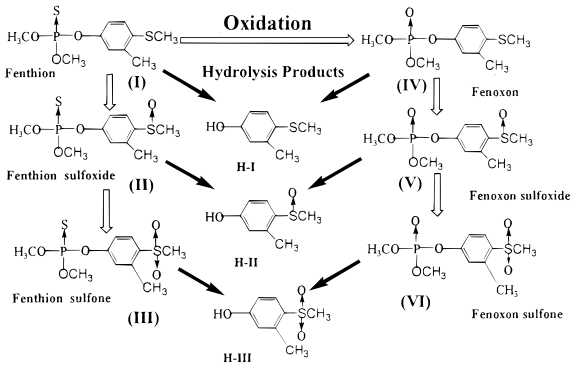

Figure 1. Fenthion (**I**), its five metabolites (**II**−**VI**) and three hydrolysis products **H-I** to **H-III**.

* Corresponding author. Tel: (416) 978-1780. Fax: (416) 978-3596. E-mail: smabury@alchemy.chem.utoronto.ca.

10.1021/jf9907539 CCC: $19.00
Published on Web 05/03/2000

chemical structures of the three hydrolysis products (**H-I**, **H-II**, and **H-III**) are also shown in Figure 1.

Several studies concerning the persistence of fenthion in the aquatic environment have been carried out. It is relatively stable under acidic conditions, and moderately stable in alkaline conditions, with the following half-lives at 22 °C: 223 days at pH 4, 200 days at pH 7, and 151 days at pH 9 (Tomlin, 1994). Fenthion degrades faster in river water (Eichelberger and Lichtenberg, 1971) than in the presence of sediment (difference in half-life was from 7 to 23 days), biodegradation being a relevant process (Walker et al., 1988). Fenthion degrades much faster under sunlight conditions than in darkness (Lartigues and Garrigues, 1995), with the following half-lives at 22 °C: 42 days in darkness and 2 days under sunlight for river water at pH 7.3; 26 days in darkness and 5 days under sunlight for seawater at pH 8.1. The half-lives of fenthion and its photooxidation product, fenthion sulfoxide, in estuarine waters were reported to be 4.6 and 6.9 days, respectively (Lacorte et al., 1995).

We hypothesized photodegradation of fenthion in natural waters would lead to similar degradation products (Huang and Mabury, 2000a) which are more toxic than the initial insecticide. Fenthion provides an excellent structural template in order to observe the influence of oxidation on hydrolysis rates. We further hypothesized the oxidized metabolites would be more susceptible to hydrolysis and thus yield a faster detoxification. In this study, we investigated the kinetics of hydrolysis of fenthion and its five metabolites at two pH values (pH 7 and pH 9) and three temperatures; we also identified and measured the rate of appearance of hydrolysis products in order to determine the reaction mechanism more accurately. This research work is of particular environmental significance since the pH range of most natural waters is from pH 7 to pH 9 (Huang and Mabury, 2000b). The objective of this investigation was to enhance the knowledge of the fate of fenthion and its metabolites in aqueous solutions and the hydrolysis mechanisms at different pH values.

MATERIALS AND METHODS

Chemicals. Fenthion (98%) was obtained from Chem Service (West Chester, PA). Sodium phosphate dibasic (ACS grade) and potassium phosphate (ACS grade) were obtained from ACP Chemicals, Inc. (Montreal, Quebec). Disodium tetraborate (Borax, ACS grade) was purchased from BDH Inc. (Toronto, ON). Potassium permanganate, *m*-cresol (99%), hydrogen peroxide (30%), sodium sulfate anhydrous (ACS grade), and silica gel (70−230 mesh, 60 Å) were obtained from Aldrich Chemical Co. (Oakville, ON). Selenium dioxide (99%) was obtained from BPH Chemicals Ltd. (Poole, England). Sulfuric acid (ACS grade) was purchased from J.T. Baker Inc. (Phillipsburg, NJ). Methyl disulfide (98%) was obtained from MC/B (Norwood, OH). Acetonitrile (HPLC grade), water (HPLC grade), methanol (HPLC grade), hexanes (ACS grade), ethyl acetate (ACS grade), and acetic acid (99.7%) were purchased from Caledon (Georgetown, ON). Other metabolites and hydrolysis products were synthesized from the following procedures.

Synthesis of Compounds. The metabolites of fenthion (**II**−**VI**), **H-I**, **H-II,** and **H-III** were synthesized through the following procedures. These compounds were then purified through silica gel column chromatography with hexane and ethyl acetate at varying ratio as solvent. The chemical structure of each compound was confirmed by GC-MS. A Perkin-Elmer Autosystem XL GC with a MDN-5 column (30 m × 0.25 mm, 0.25 μm film thickness) coupled to a PE TurboMass mass spectrometer in electron impact (EI, 70 eV) mode was used for obtaining mass spectra of synthesized compounds. The UV spectra of each compound was obtained on a Waters HPLC system containing a diode array detector (model 996).

II, **III**, and **VI** were prepared from fenthion following the general procedure reported by Cabras et al. (1991) with some modification.

*Fenthion Sulfoxide (**II**).* 0.15 M H_2O_2/SeO_2 in methanol solution was added dropwise to a solution of fenthion in methanol at room temperature with a magnetic stirrer. The reaction mixture was then stirred for 15 min, diluted with a saturated sodium chloride solution and extracted with chloroform. The chloroform layer was cleaned up and dehydrated with anhydrous sodium sulfate, and subsequently removed by rotary evaporation to give the crude fenthion sulfoxide as yellow oil.

*Fenthion Sulfone (**III**).* 0.15 M $KMnO_4$ in methanol was added to a solution of fenthion in acetic acid at room temperature with a magnetic stirrer. The reaction mixture was then stirred for 12 h, diluted with 35 mL of HPLC grade water and extracted with chloroform. The chloroform layer was neutralized with $NaHCO_3$, cleaned up, and dehydrated with anhydrous sodium sulfate. After evaporation of solvent, crude **III** appeared as a white solid.

*Fenoxon sulfone (**VI**)* was obtained by procedures similar to those used for fenthion sulfone: 0.20 M $KMnO_4$ in methanol was added to a solution of fenthion in acetic acid. The reaction mixture was then stirred for 16 h.

Intermediate to the synthesis of fenoxon (**II**), 3-methyl 4-methylthiophenol (**H-I**), was prepared by reaction of *m*-cresol with methyl disulfide (Ho et al., 1987). The concentrated sulfuric acid was added to a mixture of *m*-cresol and methyl disulfide, and the reaction mixture was stirred for 6 h in an ice bath. The solution was diluted with HPLC grade water and extracted two times with chloroform. The organic layers were neutralized with $NaHCO_3$, washed with water, and dehydrated with anhydrous sodium sulfate. Under reduced pressure of 10 Torr, the organic solvent and the remaining *m*-cresol were removed to give crude 3-methyl-4-methylthiophenol. The chemical structure was confirmed by GC-MS with *m*/*z* 154 (M^+, 100), 139 (65), 107 (100), 95 (32), and 77 (23), ^{1}H NMR δ_H 2.33 (S, 3H), 2.40 (S, 3H), 5.56 (S, 1H), 6.69 (d, 2H), and 7.15 (d, 1H), and UV spectra with a specific peak at 250 nm.

*Fenoxon (**IV**)* was prepared by reaction of 3-methyl-4-methylthiophenol (MMTP) with dimethyl phosphorochloride in acetone in the presence of sodium carbonate following the general procedure reported by Green et al. (Green et al., 1987). MMTP was put in acetone, and Na_2CO_3 and dimethyl phosphorochloride were added. The reaction mixture was then refluxed at 60−70 °C water bath for 5 h. After acetone was removed, the solution was diluted and extracted with chloroform. The organic layer was washed with water and dehydrated with anhydrous sodium sulfate. A rotary evaporator was used to obtain crude **IV** liquid.

*Fenoxon sulfoxide (**V**)* was obtained by the same procedures as those used for fenthion sulfoxide reported by Cabras et al. (1991).

The other two hydrolysis products of its metabolites, 3-methyl-4-methylsulfinylphenol (**H-II**) and 3-methyl-4-methylsulfonylphenol (**H-III**), were prepared by hydrolysis of fenthion sulfoxide and fenoxon sulfone under strong basic conditions. Fenthion sulfoxide or fenoxon sulfone was added in 1 N NaOH ethanol solution (ethanol:H_2O = 1:1). The reaction mixture was agitated under magnetic stirring for 8 h in 50−60 °C water bath, and then 2.5 N HCl was added to neutralize the mixture. The mixture was diluted with saturated sodium chloride and extracted with ethyl acetate. The organic layer was washed with water and dehydrated with anhydrous sodium sulfate. The rotary evaporator was used to turn crude **H-II** and **H-III** into crystals. The chemical structure of **H-II** was identified by GC-MS with *m*/*z* 186 (M^+, 100), 171 (95), 123 (39), 107 (56), and 77 (40) and UV spectra with a specific peak at 240 nm. The chemical structure of **H-III** was identified by GC-MS with

Table 1. HPLC Analysis Conditions

analysis compound	mobile phase (ACN:H_2O)	λ (nm)	retention time (min)
fenthion (**I**), (**H-I**)	75:25	250	**I**, 7.5; **H-I**, 3.9
fenoxon (**IV**), (**H-I**)	65:35	250	**IV**, 5.7; **H-I**, 4.8
fenthion sulfoxide (**II**), (**H-II**)	35:65	245	**II**, 18; **H-II**, 3.6
fenoxon sulfoxide (**V**), (**H-II**)	30:70	245	**V**, 6.2; **H-II**, 4.2
fenthion sulfone (**III**), (**H-III**)	55:45	225	**III**, 8.3; **H-III**, 3.7
fenoxon sulfone (**VI**), (**H-III**)	40:60	225	**VI**, 5.6; **H-III**, 4.5
H-I	65:35	250	**H-I**, 4.8
H-II; **H-III**	30:70	240	**H-II**, 4.2; **H-III**, 5.7

m/z 170 (M^+, 35), 155 (87), 154 (100), 139 (42), 107 (23), and 109 (24), and UV spectra with a specific peak at 240 nm.

Experimental Procedures. Buffer solutions were utilized for determination of hydrolysis kinetics in order to ensure consistent pH over the course of the experiment given the production of weak acids following cleavage of the ester bond; our primary aim was elucidation of reaction kinetics and mechanism which required strict control of solution conditions. Individual solutions were prepared to pH 7 (0.025 M KH_2PO_4 and 0.025 M Na_2HPO_4) or pH 9 (0.01 M Borax), which were adjusted with 0.1 M HCl and 0.1 M NaOH at different temperatures of 25, 50, or 65 °C; the water used was filter sterilized (0.45 μm) to preclude microbial degradation. Individual solutions of **I**−**VI,** 50−100 μM in duplicate, at pH 7 and pH 9 buffers were prepared in 15 mL screw-top test tubes which were wrapped with foil to preclude photolysis. The test tubes were placed into a water bath at the specified temperatures. Samples at appropriate time intervals were taken for analysis of the organophosphate and corresponding hydrolysis product; each time point was determined in triplicate.

Analysis by HPLC. I−**VI** and the primary hydrolysis products (**H-I** to **H-III**) concentration were determined by direct injection in an HPLC. A complete Waters HPLC system was employed with a Waters 600 pump and controller and a Waters 486 tunable absorbance detector. Separations were performed using a reverse-phase Econosil C18 column (Alltech) 25 cm long with an inner diameter of 4.6 mm and 5 μm particle size. Concentrations (50−100 μM) were chosen so that aqueous samples were analyzed directly, without preconcentration or sample purification. The isocratic conditions were carried out with acetonitrile−water in various ratios at a flow rate of 1.0 mL/min; HPLC analysis conditions including mobile phase, detection wavelength, and retention time are shown in Table 1. Calibration was performed daily using external standards.

RESULTS AND DISCUSSION

Effect of pH on Hydrolysis. Chemical hydrolysis of fenthion and its metabolites was investigated using buffered solutions at pH 7 and pH 9, a typical range of natural waters. All plots of $\ln(C/C_0)$ (C_0 is the reactant concentration at $T = 0$, C is the reactant concentration at various times) versus time were linear at pH 7 and pH 9, indicating that the reaction tends to be pseudo first order as indicated in Figure 2. The hydrolysis rate constant and half-life (Table 2) indicate the relative stability of fenthion and its metabolites in a neutral medium. The rate constant were reproducible with a relative error less than 2%. The stability of these compounds decreased as the pH increased from pH 7 to pH 9, and the hydrolysis rate constants were higher at pH 9 than that at pH 7 for fenthion and each of the metabolites investigated. At 50 °C, the hydrolysis half-life varied from 4.86 days for fenthion to 1.55 days for fenoxon sulfone at pH 7, and from 4.80 days for fenthion to 0.55 day for fenoxon sulfone at pH 9. Chemical hydrolysis of fenthion and its metabolites at 25 and 65 °C was also investigated using the same buffered solutions. As a result, the hydrolysis rate constant and half-life indicate the same relative stability in a neutral medium, which is shown in Table 2. Hydrolysis proceeded at higher rates under alkaline conditions, suggesting that the reaction was more effectively catalyzed by hydroxide ions than by neutral water molecules or hydronium ions; this was more apparent for the oxon derivatives. However, the slight difference of rate constants for fenthion at pH 7 and 9 indicated no significant influence of pH on the hydrolysis rate of fenthion over this pH range. The relatively rapid

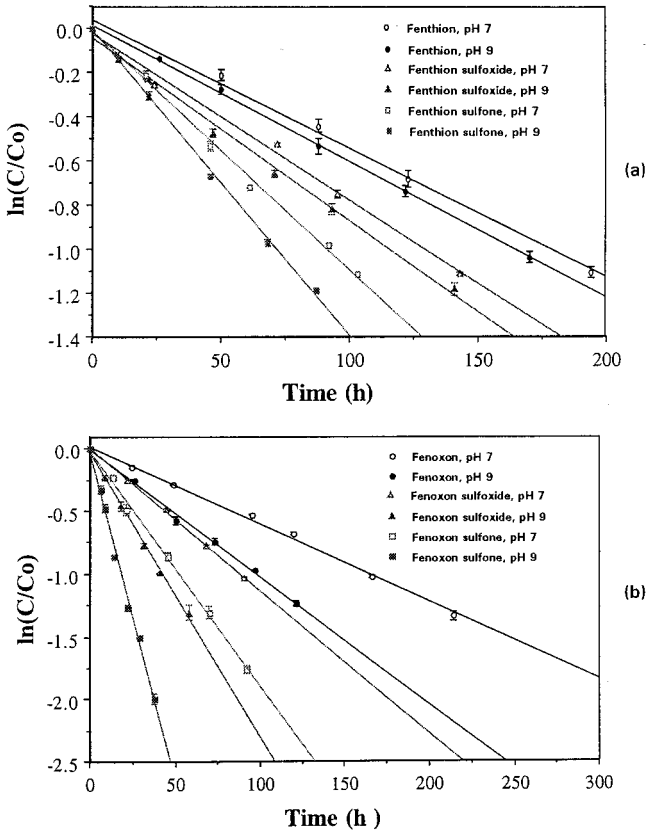

Figure 2. 2. Hydrolysis rate of **I**−**III** at 50 °C and pH 7 and pH 9 (a) and **IV**−**VI** at 50 °C and pH 7 and pH 9 (b); $N = 2$.

Table 2. Hydrolysis Rate Constant *k* and Half-life $t_{1/2}$ at Different Temperatures[a]

temp	compound	k (day^{-1}) at pH 7	$t_{1/2}$ (days) at pH 7	k (day^{-1}) at pH 9	$t_{1/2}$ (days) at pH 9
25 °C	fenthion	0.0117	59.0	0.0125	55.5
	fenthion sulfoxide	0.0169	41.0	0.0200	34.7
	fenthion sulfone	0.0278	24.9	0.0461	15.0
	fenoxon	0.0149	46.5	0.0213	32.5
	fenoxon sulfoxide	0.0326	21.3	0.0425	16.3
	fenoxon sulfone	0.0420	16.5	0.0730	9.50
50 °C	fenthion	0.143	4.86	0.144	4.80
	fenthion sulfoxide	0.181	3.83	0.193	3.59
	fenthion sulfone	0.257	2.69	0.331	2.11
	fenoxon	0.146	4.74	0.247	2.80
	fenoxon sulfoxide	0.314	2.55	0.557	1.25
	fenoxon sulfone	0.446	1.55	1.250	0.55
65 °C	fenthion	0.545	1.27	0.583	1.19
	fenthion sulfoxide	0.550	1.26	0.725	0.95
	fenthion sulfone	1.08	0.64	1.43	0.48
	fenoxon	0.602	1.15	0.766	0.90
	fenoxon sulfoxide	1.02	0.68	2.66	0.26
	fenoxon sulfone	1.84	0.38	6.30	0.11

[a] The data of measured rate constants were reproducible with relative error less than 2%.

Table 3. Activation Energy E_a, Frequency Factor A, and Activation Entropy $\Delta S^{\ddagger}$

compound	E_a (kcal/mol)	A (s^{-1})	$\Delta S^{\ddagger}$ (cal/(mol K))
at pH 7			
fenthion	19.2	1.65×10^7	−27.7
fenthion sulfoxide	17.4	1.31×10^6	−32.7
fenthion sulfone	18.6	1.28×10^7	−28.3
fenoxon	18.4	5.05×10^6	−29.9
fenoxon sulfoxide	17.3	1.74×10^6	−32.1
fenoxon sulfone	18.8	2.97×10^7	−26.4
at pH 9			
fenthion	19.2	1.61×10^7	−27.9
fenthion sulfoxide	17.9	3.00×10^6	−31.2
fenthion sulfone	16.7	1.33×10^6	−32.6
fenoxon	18.1	4.11×10^6	−30.4
fenoxon sulfoxide	20.6	5.52×10^8	−20.6
fenoxon sulfone	22.1	1.40×10^{10}	−11.7

fenthion oxidation derivatives perhaps explains the lack of literature citations for these compounds in field waters.

Effect of Temperature on Hydrolysis. At 25 °C, the half-life of fenthion is 59 days at pH 7 and 55.5 days at pH 9, which is relatively shorter in comparison with half-lives of fenthion reported at 22 °C: 223 days at pH 4, 200 days at pH 7, and 151 days at pH 9 (Tomlin, 1994) and half-lives of fenthion at 23.5 °C: 101.8 days at pH 7 and 101.7 days at pH 9 (Wang et al., 1989). The slight difference of half-lives of fenthion at pH 7 and pH 9 reported by Wang et al. (1989) is consistent with our results. The half-lives of fenthion as 189 days at 6 °C and 71 days at 22 °C in darkness for Mill-Q water at pH 6.1 was reported by Lartiges and Garrigues (Lartigues and Garrigues, 1995). The half-life of fenthion in buffered aqueous media is much longer than in environmental water systems, such as half-lives of 26 days at 22 °C in darkness, 5 days under sunlight condition for seawater at pH 8.1 (Lartigues and Garrigues, 1995); persistence of up to 4 weeks in river water (Eichelberger and Lichtenberg, 1971); half-life of 4.6 days in estuarine waters (Lacorte et al., 1995). Other reaction pathways to degrade organophosphate pesticides in natural waters such as oxidation, photolysis, and microbial degradation in addition to hydrolysis would contribute to increase the overall transformation rate of fenthion.

Using the data shown in Table 2, the activation energy can be derived from the Arrhenius equation:

$$K = \mathrm{A}e^{-E_a/RT} \quad (1)$$

where k ($time^{-1}$) is the rate constant at temperature T, A is the frequency factor ($time^{-1}$), E_a is the activation energy, and R is the gas constant. The activation energy (E_a) and frequency factor (A) were calculated using the Arrhenius equation. E_a and A may be determined with an accuracy of about 95% since the relative error in the rate constant was less than 2% (Mabey and Mill, 1978). The range of E_a was from 17.3 kcal/mol for fenoxon sulfoxide to 19.2 kcal/mol for fenthion at pH 7 and from 16.7 kcal/mol for fenthion sulfone to 22.1 kcal/mol for fenoxon sulfone at pH 9. These E_a values were consistent with the activation energies for a range of organophosphate pesticide hydrolysis, ranging from 14 to 22 kcal/mol (Freed et al., 1979). Although pH determines the hydrolytic mechanism, its effect on E_a is less clear since E_a depends both on the structure of the molecule and on the mechanism. The magnitude of the activation energy provides an indication of the sensitivity of the reaction to temperature change.

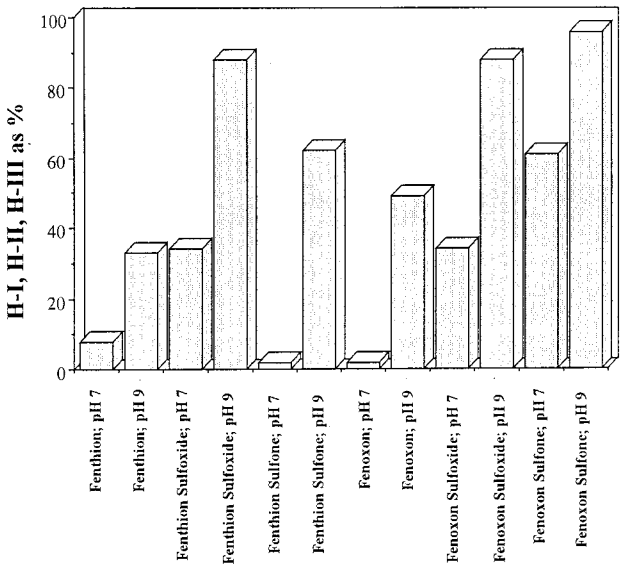

Figure 3. At 50 °C, the percentage of fenthion and its metabolites converted into **H-I** to **H-III** at the first time point.

Fenoxon sulfone and fenoxon sulfoxide at pH 9 have the highest rate constants in comparison with other metabolites at different temperatures. However, their activation energies were also highest among the compounds investigated with 22.1 and 20.6 kcal/mol, respectively. So, the highest rate constants were due to the frequency factors A. The frequency factor (A) of **V** and **VI** at pH 9 were 5.52×10^8 and 1.40×10^{10} s^{-1} respectively; these values were larger than the frequency factors for the other compounds. The relatively higher frequency factor is due to the entropy effect based on the activated complex theory (Ruff and Csizmadia, 1994). To prove this point, the activation entropies ($\Delta S^{\ddagger}$) were calculated using the equation of Ruff and Csizmadia (1994); all values are shown in Table 3 (the relative error of activation entropies was less than 5%). The entropy of activation for fenthion were −27.7 and −27.9 cal/(mol K) at pH 7 and 9, which is higher than that of **II** and **III** and due to the hydrogen bonding on the O atom of the sulfinyl and sulfonyl group with water at the activated complex. As a result, the entropy of activation of **II** and **III** is decreased in comparison with **I**.

On the other hand, the entropy of activation for fenoxon and **V** and **VI** at pH 9 was apparently decreased from −30.4 cal/(mol K) for fenoxon to −20.6 and −11.7 cal/(mol K) for **V** and **VI**, respectively. This large difference presumably comes from the electrostatic force between the P atom and hydroxide ion. The strong electronegative O atom connecting to the P atom would make the phosphorus of **IV**, **V**, and **VI** more positive than that of **I**, **II**, and **III** when the S atom replaces the O atom. In addition, the strong electron-withdrawing group of sulfonyl and sulfinyl on **V** and **VI** result in the P atom being even more positive than that of **IV**. Therefore, the P atom on **V** and **VI**, with a partial positive charge, can form an ion pair with hydroxide ion through electrostatic force, which greatly decreases the entropy of reactants. Then, the entropy of activation $\Delta S^{\ddagger}$ between the entropy of the activated complex and reactants would increase; $\Delta S^{\ddagger}$ results were consistent with the frequency factor (A). This entropy effect may explain why **VI** and **V** at pH 9 with the highest activation energy (E_a) also have the highest rate constants. At pH 7, the same entropy effect was not

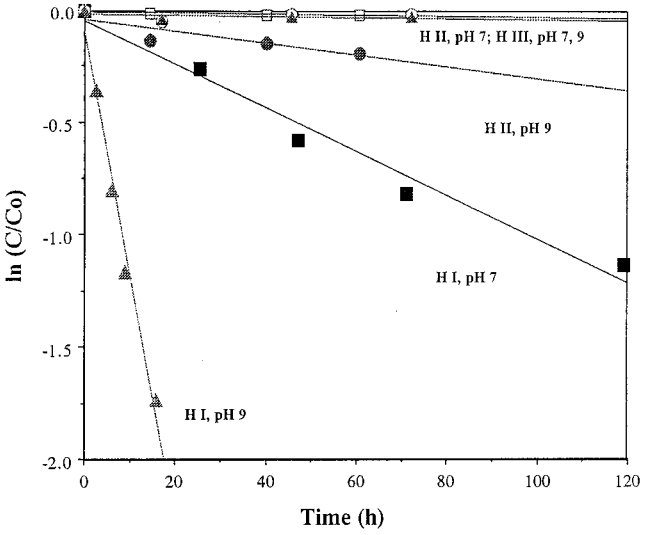

Figure 4. Hydrolysis rate of **H-I**, **H-II**, and **H-III** at 50 °C.

apparent for **IV**, **V**, and **VI** which we believe is due to the lack of an ion pair formed with the neutral water molecule.

Stability of the Hydrolysis Products. From their chemical structures in Figure 1, **H-I**, **H-II**, and **H-III** are the hydrolysis product of **I** and **IV**, **II** and **V**, and **III** and **VI**, respectively. These products result from hydrolysis of the parent compound via hydroxide ion or water attack at the P atom and can be determined simultaneously following direct injection into the HPLC. The percentage of the reactant converted into the hydrolysis product at 50 °C is shown in Figure 3; percentage (%) conversion was calculated at the second time point. The percentage is higher at pH 9 than at pH 7, which indicates that there possibly exist different mechanisms at different pHs. At 50 °C, there are 88% and 62% of the hydrolysis products for **II** and **III** at pH 9, and only 34% and 2% at pH 7. There are 88% and 96% of the hydrolysis products for **V** and **VI** at pH 9, and only 34% and 61% of the hydrolysis products at pH 7. Even in neutral medium, **H-III** is still the primary product through water molecules-catalyzed hydrolysis of fenoxon sulfone. At pH 9, there are 33% **H-I** and 49% **H-I** for fenthion and fenoxon at 50 °C, and only 8% and 2% at pH 7.

It was necessary to determine the stability of three hydrolysis products at pH 7 and pH 9. Figure 4 shows the stability of three hydrolysis products at 50 °C. It can be seen that **H-III** is stable at pH 7 as well as at pH 9, and **H-II** is stable only at pH 7. Also, **H-II** is relatively stable at pH 9 with a first-order rate constant of 0.0634 day^{-1}. **H-I** is not stable at pH 7 or at pH 9, with a first-order rate constant of 0.232 day^{-1} and 2.59 day^{-1}, respectively, which are higher than the hydrolysis rate constant of fenthion and fenoxon at similar pH. This may explain in part why the percentage of **H-I** is lower than that of the other two products.

Hydrolysis Mechanism. Fenthion and its metabolites are thiophosphate or phosphate esters. The hydrolysis of such compounds occurs through reaction with a nucleophile by nucleophilic substitution (S_N2), both at the phosphorus atom with an alcohol moiety or a phenol derivative as the leaving group and at the carbon bound to the oxygen of an alcohol moiety with the diester as the leaving group (Schwarzenbach et al., 1993). The reaction rate of the S_N2 reaction depends on the electrophilic ability of the central atom and on the presence of a good leaving group. The hydrolysis mechanisms of fenthion and its metabolites are fundamen-

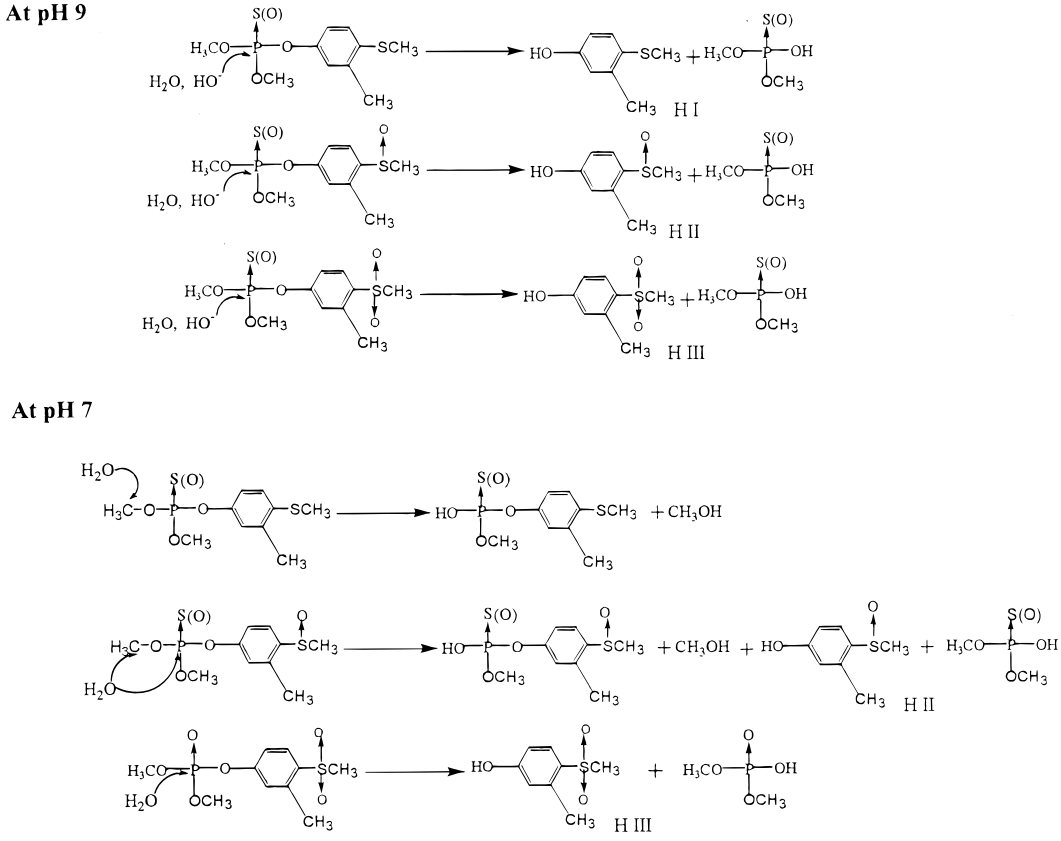

Figure 5. Proposed primary hydrolysis pathway for **I** to **VI** at pH 7 and pH 9.

tally different at pH 7 and pH 9. At pH 9, hydrolysis of these compounds results in the formation of phenol derivatives and dialkylphosphoric acid because OH^- is about 10^8 times stronger than H_2O as a nucleophile toward P atom (Barnard et al., 1961). However, the neutral water molecule can also act as a nucleophile toward the P atom at pH 7, which is shown clearly on the Figure 3. The formation of the phenol derivative is presumably due to the combined attack of OH^- ion and H_2O at the phosphorus atom, which results in cleavage of the P−O aryl bond. Since **H-I** is not stable at pH 9, the S_N2 reaction occurring at the P atom is still possibly the primary mechanism for fenoxon and fenthion even if the percentage of product was lower than that of other metabolites. The proposed reaction mechanism is shown in Figure 5. This mechanism is similar to that reported for parathion which showed both dearylation and dealkylation important at different pH values (Weber, 1976).

The percentages of phenol derivative products of fenoxon (**IV**) and its oxidized compounds (**V, VI**) are higher than those of fenthion and its oxidized compounds (**II, III**) because of the increased electrophilicity of the P atom when an O atom replaces an S atom. On the other hand, **H-III** is a better leaving group than **H-II** or **H-I** because the negative charge on the phenolic oxygen atom after the P−O bond cleavage can delocalize on the two oxygen atoms on the sulfur atom. Similarly, **H-II** is a better leaving group than **H-I**. Even at pH 7, there is 62% of **H-III** for **VI** due to the good leaving group (50 °C), which indicates that the S_N2 reaction occurring at the phosphorus atom with H_2O as nucleophile is still the primary mechanism of hydrolysis (Figure 5).

Under neutral conditions, the amount of phenol derivative products is lower than that under alkaline conditions because water molecules are weaker nucleophiles than hydroxide ions. The primary neutral reaction mechanism is presumably through dealkylation of organophosphate pesticides, which is associated with the reaction of a water molecule at the alkyl carbon atom, followed by cleavage of the C−O bond to form the corresponding alcohol (Trucklik and Kovacicova, 1977); we were unable to determine the products due to lack of standards for the resulting aryl monoalkyl phosphoric acid derivative. The dealkylation of organophosphate insecticides has previously been observed in buffered distilled water (Greenhalgh et al., 1980) and in natural water systems (Maguire and Hole, 1980). We propose the primary hydrolysis mechanism of fenthion, fenoxon, and fenthion sulfone at pH 7 is an S_N2 reaction occurring at the carbon bound to the oxygen to form methanol (Figure 5). If a good leaving group is present, the neutral reaction may proceed by both reaction mechanisms, that is, C−O as well as P−O cleavage (Schwarzenbach et al., 1993). At 50 °C, there are still 34% of **H-II** in **II** and 34% of **H-II** in **V** at pH 7. Both reaction mechanisms therefore exist under neutral conditions for **II** and **V** (Figure 5).

CONCLUSIONS

The rate constants, half-lives, activation energies (E_a), and proposed hydrolysis mechanisms presented clearly indicate pH and structure have a large influence on the rate and mechanism of hydrolysis. Furthermore, these results support the hypothesis that photooxidation of fenthion results in intermediates that are rapidly degraded through hydrolytic cleavage. These hydrolysis products are generally nontoxic and indicate the importance of the role sunlight plays in the natural cleansing of field waters. This investigation can be used to enhance the predictive capabilities of determining persistence of related insecticides by including a more accurate model of hydrolysis to the large knowledge base available for predicting volatilization and sorption.

LITERATURE CITED

Aly, O. A.; Badawy, M. I. Hydrolysis of organophosphate insecticides in aqueous media. *Environ. Int.* **1982**, *7*, 373−377.

Barnard, P. W.; Burton, C. A.; L'lewellyn, D. R.; Vernon, C. A.; Welch, V. A. The reactions of organic phosphates. Part, V. The hydrolysis of triphenyl and trimethyl phosphates. *J. Chem. Soc.* ***1961***, 3, 2670−2676.

Cabras, P.; Plumitallo. A.; Spanedda, L. High-performance liquid chromatographic separation of fenthion and its metabolites. *J. Chromatogr.* **1991**, *540*, 406−410.

Cabras, P.; Garau, V. L.; Melis, M.; Pirisi, F. M.; Spanedda, L. Persistence and fate of fenthion in olives and olive products *J. Agric. Food Chem*. **1993**, *41*, 2431−2433.

Cowart, P. R.; Bonner, F. L.; Epps, E. A. Rate of hydrolysis of seven organophosphate pesticides. *Bull. Environ. Contam. Toxicol.* **1971**, *6*, 231−234.

Draper, W. M.; Crosby, D. G. Solar Photooxidation of Pesticides in Dilute Hydrogen Peroxide. *J. Agric. Food Chem*. **1984**, *32*, 231−237.

Eichelberger, J. W.; Lichtenberg, J. J. D. Persistence of pesticides in river water. *Environ. Sci. Technol.* **1971**, *5*, 541−544.

FAO/WHO. *Pesticides residues in Food*, 1971 Evaluations; FAO/WHO: Roma **1973**, 110−149.

Freed, V. H.; Chlou, C. T.; Schmeding, D. W. Degradation of selected organophosphate pesticides in water and soil. *J. Agric. Food Chem*. **1979**, *27*, 706−708.

Green, M. B.; Hartley, G. S.; West, T. F. *Chemicals for crop improvement and pest management*, 3rd ed.; Pergamon Press: New York, 1987; pp 93−95.

Greenhalgh, R.; Dhawan, K. L.; Weinberger, P. Hydrolysis of fenitrothion in model and natural aquatic systems. *J. Agric. Food Chem*. **1980**, *28*, 102−105.

Ho, H. W.; Liu, Z. J.; Zou, D. P.; Yan, G. Methylthiolation of phenols (I). Synthesis of 3-methyl-4-(methylthio)phenol. *Huazhong Shifan Daxue Xuebao, Zirankexueban*. **1987**, *21*, 367−375.

Huang, J.; Mabury, S. A. The role of carbonate radical in limiting the persistence of sulfur containing chemicals in sunlit natural waters. *Chemosphere* **2000a**, *41*, 79−86.

Huang, J.; Mabury, S. A. Steady-state concentrations of carbonate radical in field waters. *Environ. Toxicol. Chem*. **2000b**, in press.

Kamrin, M. A. *Pesticides Profiles: Toxicity, Environmental impact, and Fate.* CRC Lewis Publishers: Boca Raton, FL, 1997; pp 180−184.

Lacorte, S.; Lartigue, S. B.; Garrigues, P.; Barcelo, D. Degradation of organophosphorous pesticides and their transformation products in estuarine waters. *Environ. Sci. Technol.* **1995**, *29*, 431−438.

Lacorte, S.; Barcelo, D. Rapid Degradation of Fenitrothion in Estuarine Waters. *Environ. Sci. Technol.* **1994**, *28*, 1159−1163.

Lartigues, B. S.; Garrigues, P. P. Degradation kinetics of organophosphorous and organonitrogen pesticides in different waters under various environmental conditions. *Environ. Sci. Technol.* **1995**, *29*, 1246−1254.

Mabey, W.; Mill, T. Critical review of hydrolysis of organic compounds in water under environmental conditions. *J. Phys. Chem. Ref. Data* **1978**, *7*, 383−415.

Maguire, R. J.; Hole, E. J. Fenitrothion sprayed on a pond: kinetics of its distribution and transformation in water and sediment. *J. Agric. Food Chem*. **1980**, *28*, 372−378.

Minelli, E. V.; Cabras, P.; Angioni, A.; Garau, V. L.; Melis, M.; Pirisi, F. M.; Cabitza, F.; Cubeddu, M. Persistence and Metabolism of Fenthion in Orange Fruit. *J. Agric. Food Chem*. **1996**, *44*, 936−939.

Ohkawa, H.; Mikami, N.; Miyamoto, J. Photodecomposition of sumithion [*O, O*-dimethyl-*O*-(3-methyl-4-nitrophenyl)-phosphorothioate]. *Agric. Biol. Chem*. **1974**, *38*, 2247−2255.

Ruff, F.; Csizmadia, I. G. *Organic reaction*; Elsevier: New York, 1994; pp 132−134.

Ruzicka, J. H.; Thomson, J. H.; Wheals, B. B. The gas-chromatographic examination of organophosphorous pesticides and their oxidation products. *J. Chromatogr*. **1967**, *30*, 92−97.

Schwarzenbach, R. P.; Gschwend, P. M.; Imboden, D. M. *Environmental organic chemistry*; John Wiley & Sons: New York, 1993; pp 372−399.

Tomlin, C. *The pesticide Manual*; Crop Production Publications: New York, 1994; pp 451−452.

Trucklik, S.; Kovacicova, J. *Fenitrothion symposium*, Ottawa, Canada, April, 1977; NRC Publication No. NRCC 16-73.

Wang, T. C.; Lenahan, R. A.; Tucker, J. W., Jr. Deposition and persistence of aerially applied fenthion in a florida estuary. *Bull. Environ. Contam. Toxicol*. **1987**, *38*, 226−231.

Wang, T. C.; Kadiac, T.; Lenahan, R. Persistence of fenthion in aquatic environment. *Bull. Environ. Contam. Toxicol*. **1989**, *42*, 389−394.

Walker, W. W.; Cripe, C. R.; Pritchard, P. H.; Bourquin, A. W. Biological and abiotic degradation of xenobiotic compounds in *in Vitro* estaurine water and sediment/water systems. *Chemosphere* **1988**, *17*, 2255−2270.

Weber, K. Degradation of parathion in seawater. *Water Res*. **1976**, *10*, 237−241.

Weerasinghe, C. A.; Lewis, D. O.; Mathews, J. M.; Jeffcoat, A. R.; Troxler, P. M.; Wang, R. Y. Aquatic Photodegradation of Albendazole and Its Major Metabolites. 1. Photolysis Rate and Half-Life for Reactions in a Tube. *J. Agric. Food Chem*. **1992**, *40*, 1413−1418.

Received for review July 9, 1999. Revised manuscript received February 28, 2000. Accepted March 13, 2000. This research work was supported by the National Science and Engineering Research Council (NSERC) and Dupont Canada. We appreciate the contribution by Perkin-Elmer toward the creation of the Analytical Lab for Environmental Science Research and training (ANALEST) which was utilized significantly in this investigation.

JF9907539