Alkaline Hydrolysis of Some Pyrethroid Insecticides

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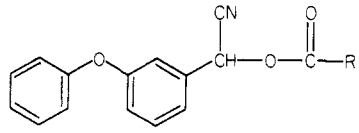
The mechanism of hydrolysis of the pyrethroids fenvalerate and cypermethrin under alkaline conditions has been shown to be similar to that of simple aliphatic esters: the rate-determining step is nucleophilic attack by a hydroxyl group. The final products of reaction have been identified as the corresponding acid and 3-phenoxybenzaldehyde (the latter derived from the fast decomposition of the cyanohydrin intermediate). This simple mechanism is valid only under low concentrations of pyrethroid ($\leq 10^{-5}$ M). At higher concentrations another reaction sets in, between 3-phenoxybenzaldehyde and unreacted pyrethroid, leading to the formation of a benzoin ester derivative.

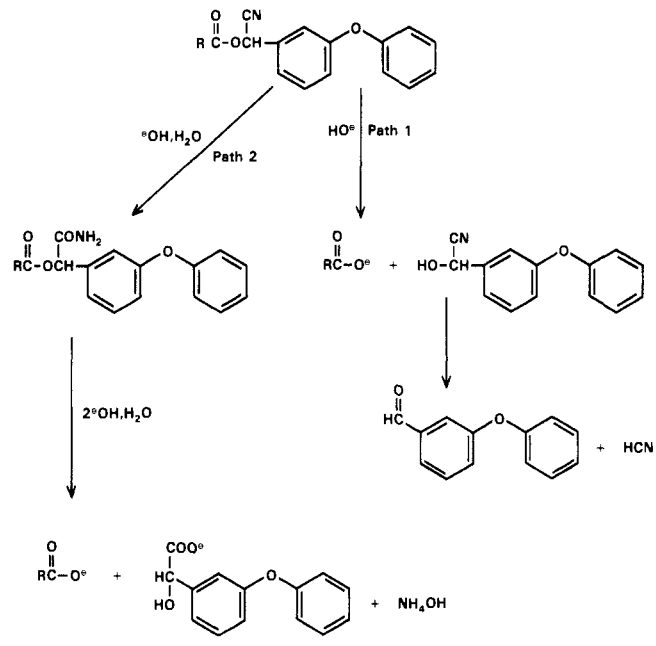
Fenvalerate and cypermethrin are widely used pyrethroid insecticides having the general structure (I)



I

Under alkaline conditions, either ester or nitrile hydrolysis can occur (Scheme I). In ester hydrolysis (path 1) the expected products of reaction are the acid, $RCOO^-$, and 3-phenoxybenzaldehyde derived from the fast decomposition of the cyanohydrin intermediate. The first product of nitrile hydrolysis (path 2) should be the primary amide, which can in turn be further hydrolyzed to give again $RCOO^-$ and 3-phenoxymandelic acid. As the alkaline hydrolysis of pyrethroids has not been reported in the literature, a knowledge of the products and the route or routes by which they are formed is of interest. In this study, we report the alkaline hydrolysis of IA [*R* = 1-(4-chlorophenyl)-2-methylpropyl] and IB [R = 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropyl]. IA is the (*S*)[*S*] optical isomer of fenvalerate while IB is the cis-2 isomer pair of enantiomers of cypermethrin. We also examine a reaction between these pyrethroids and 3-phenoxybenzaldehyde under basic conditions.

Scheme I



MATERIALS AND METHODS

Chemicals. Inorganic chemicals were of analytical grade. Deionized, distilled water was used througout. Dioxane was purified by passing over two columns (100 × 2.5 cm^2) of activated charcoal (mesh size: 6–12) and was stored at −10 °C in the dark. IA and IB were more than 98% pure.

Kinetics. A 0.5-mL sample of a stock solution of pyrethroid (about 10^{-3} M) in dioxane was added to 24.5 mL of purified dioxane in a 100-mL conical flask, maintained at the reaction temperature (±0.1 °C). Water (24.5 mL) was then added, and the clear solution was allowed to equilibrate to the reaction temperature for 30 min. At time zero 0.5 mL of a known molarity (0.05–1.5 M) of sodium hydroxide in water was added and the flask was shaken to ensure proper mixing. Sampling of the reaction mixture was carried out at appropriate time invervals. Samples (1 mL) were removed and placed in high-performance liquid chromatography (HPLC) sample vials containing enough dilute sulfuric acid to quench the reaction. The sample vials also contained 100 μL of an internal standard that consisted of about 80 ppm of hexachlorobenzene in spectroscopically pure acetonitrile.

The areas (*A*) of the reactant and product peaks were recorded as a function of time, and rate constants were obtained by plotting ln $(A_\infty - A_t)$ against time. The plots were linear for at least two half-lives.

Chromatography. The reacting pyrethroid and the corresponding products were analysed directly by HPLC. The separation was carried out on a LiChrosorb RP 18 column (20 cm × 4.5 mm i.d.; particle size 10 μm), eluted with acetonitrile–water (1:1 by volume for the first 8 min and 2:5 by volume for the rest of the time) at 1.5 mL/min. The column was incorporated in a Hewlett-Packard Model 1084B equipped with a variable-wavelength detector. Figure 1 shows the chromatogram from the hydrolysis of IA by 0.005 M sodium hydroxide at 40 °C; the sample was quenched 1.5 min after the reaction had started.

Reaction of IA or IB with 3-Phenoxybenzaldehyde. Pyrethroid (4×10^{-3} M) and 3-phenoxybenzaldehyde (5×10^{-3} M) were dissolved in 25 mL of dioxane contained in a 100-mL conical flask. Twenty-five milliliters of water was then added together with enough 2 M sodium hydroxide to bring the pH of the solution to about 14. After the reaction mixture had stood for 6 h at room temperature in the dark, it was neutralized with sulfuric acid. Most of the solvent was removed by using a rotary evaporator, while the remaining traces of water were removed by

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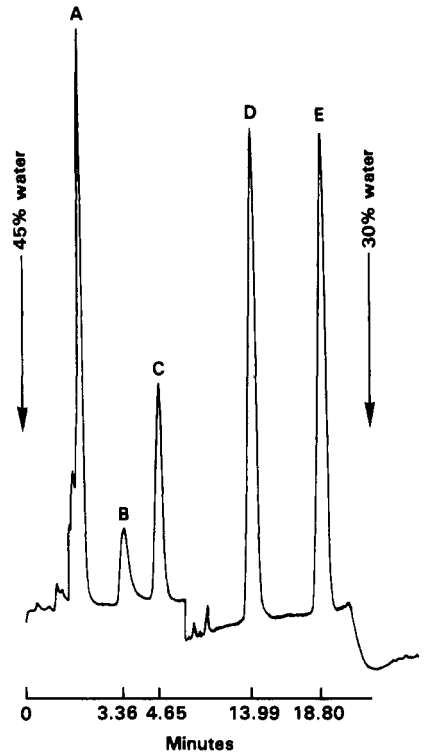


Figure 1. Typical chromatogram from the hydrolysis of the (*S*)[*S*] optical isomer of fenvalerate by 5×10^{-3} sodium hydroxide at 40 °C in dioxane–water (1:1 by volume), 1.5 min after the start of reaction. A, Solvent response; B, 2,2-dimethyl-3-(2,2-dichlorovinyl)cyclopropanecarboxylic acid; C, 3-phenoxybenzaldehyde; D, hexachlorobenzene; E, reactant pyrethroid (IA).

freeze-drying. Products were then purified by TLC, using Merck RP-8 plates F-254 and the solvent mixture acetonitrile–water (4:1 by volume) as the eluent. Under these conditions, 3-phenoxybenzaldehyde and the reactant pyrethroid coeluted with an R_f of around 0.5 while the product of reaction had an R_f of about 0.1. The band containing this product was separated from the TLC plate and extracted with acetonitrile. Solvent was finally removed by a slow stream of nitrogen. The purity of the sample was checked by HPLC using the same LiChrosorb column as before and eluting with the solvent system acetonitrile–water (4:1 by volume). Samples were then submitted for the usual spectroscopic analysis. Since these products were found to be photochemically unstable, all preparative and purification work was carried out in subdued light.

Spectroscopy. Chemical ionization mass spectra (CI-MS) were recorded with a Finnigan spectrophotometer interfaced with a data system; ammonia was used as the reagent gas. Nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a 360-MHz Fourier transform instrument; compounds were dissolved in $CDCl_3$, and tetramethylsilane was used as the internal standard. Infrared spectra (IR) were recorded on a Fourier transform instrument, and samples were deposited as a thin film on a KBr disk.

RESULTS AND DISCUSSION

The alkaline hydrolysis of the two pyrethoids studied (IA and IB) was found to proceed solely via ester cleavage (path 1 in Scheme I). Both the decomposition of the respective pyrethroid and the formation of the corresponding acid and 3-phenoxybenzaldehyde were pseudo first order. For a particular reaction, plots of ln $(A_\infty - A_t)$ with time, for the pyrethroid and the two products, were parallel within experimental error. The average of the

Table I. Hydrolysis of IB in 1:1 Dioxane–Water

temp, °C	T, K	$10^3/T$	k_{OH^-}, dm^3 mol^{-1} s^{-1}	ln k_{OH^-}
20	293	3.411	0.149	−1.90
25	298	3.354	0.182	−1.70
30	303	3.299	0.284	−1.26
35	308	3.245	0.298	−1.21
40	313	3.193	0.463	−0.770
45	318	3.143	0.640	−0.466

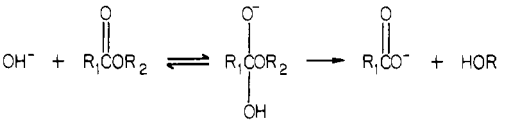
Table II. Hydrolysis of IA in 1:1 Dioxane–Water

temp, °C	T, K	$10^3/T$	k_{OH^-}, dm^3 mol^{-1} s^{-1}	ln k_{OH^-}
20	283	3.411	0.100	−2.30
25	298	3.354	0.150	−1.90
30	303	3.299	0.202	−1.60
35	308	3.245	0.228	−1.48
40	313	3.193	0.427	−0.850
45	318	3.143	0.547	−0.626

Table III. Thermodynamic Activation Parameters for IB and IA at 25 °C

compd	ΔE, kJ mol^{-1}	ln A	$\Delta S^\ddagger$, J mol^{-1} K^{-1}	$\Delta H^\ddagger$, kJ mol^{-1}
IB	45	16.4	−117	42
IA	51	18.8	−97	49

slopes of these lines gave the observed pseudo-first-order rate constants. A plot of these rate constants against hydroxide ion concentration was a straight line that passed through the origin and gave directly the second-order rate constants, k_{OH^-}, presented in Tables I and II. These rate constants are of the same order of magnitude for both IA and IB. Table III gives the thermodynamic activation parameters for the two pyrethroids. A compensatory effect of the enthalpy ($\Delta H^\ddagger$) and entropy ($\Delta S^\ddagger$) of activation is apparent and is similar to that found for the basic hydrolysis of other esters (Bruice and Fife, 1962). The absolute values for the entropy of activation of both pyrethroids can be compared with those determined for the alkaline hydrolysis of ethyl esters of the type RCOOEt in water at 25 °C; the values found (Euranto, 1969) for these compounds vary between −85 and −134 J mol^{-1} deg^{-1}. These results strongly suggest that the mechanism of hydrolysis of the pyrethroids studied is similar to that of some simple aliphatic esters, that is, the rate-determining step is the nucleophilic attack of OH^-.

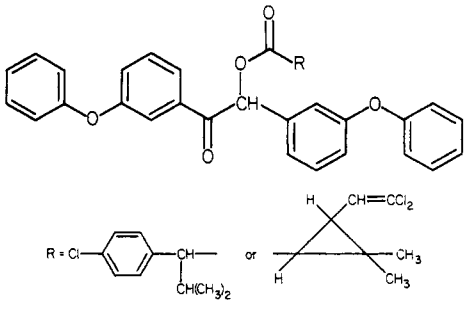


No evidence was found in this study that indicated the occurrence of path 2 in Scheme I. This is not surprising as the activation energy reported for the alkaline hydrolysis of nitriles (Zavorinu and Cavadia, 1971) is in the region of 72 kJ mol^{-1}, that is, about 21–27 kJ higher than that for the hydrolysis of IB and IA, respectively.

In the above kinetic study, it was necessary to work at low concentrations of pyrethroid (about 10^{-5} M) in order to obtain near theoretical yields (>85%) of 3-phenoxybenzaldehyde. It was discovered that at higher concentrations, aldehyde recovery was down by up to 50% and with both IB and IA two new products appeared with a longer HPLC retention time than that of either pyrethroid. As this was a clear indication of the occurrence of a reaction between 3-phenoxybenzaldehyde and the respective pyrethroid, we investigated this reaction directly and collected enough material for spectroscopic characteriza-

Figure 2. HPLC chromatogram of the two products from the reaction of IB with 3-phenoxybenzaldehyde.

tion. The HPLC chromatogram of the two products from the reaction of IB with 3-phenoxybenzaldehyde is shown in Figure 2. Two products were also found from the corresponding reaction with IA. HPLC–MS analysis showed that for both pyrethroids the two products had an identical mass spectrum. CI-MS gave molecular weight of 590 and 586 for the pair of products from IA and IB, respectively. The IR spectrum showed the presence of two strong peaks around 1701 and 1730 cm^{-1}, characteristic of the C=O stretching vibrations in benzoin benzoates (Kuebrick and Schowen, 1971). The NMR spectrum of the pair of products from IA is shown in Figure 3: 6.96 (22 H, multiplet), 6.68 and 6.65 (1 H, two singlets), 3.31 and 3.29 (1 H, two doublets), 2.35 (1 H, multiplet), 1.12 and 1.05 (3 H, two doublets), and 0.74 (3 H, two merging doublets). All these spectroscopic data are consistent with a mixture of the two diastereoisomeric forms of structure II.



The mechanism by which II is formed most likely involves the ionic intermediate III (Scheme II). The latter species can undergo an intramolecular nucleophilic attack at the ester function to give the benzoin ester II. This mechanism is similar to that proposed by Kuebrick and Schowen (1971) in their study of the reaction of a α-benzoyloxycyano carbanion intermediate with a variety of

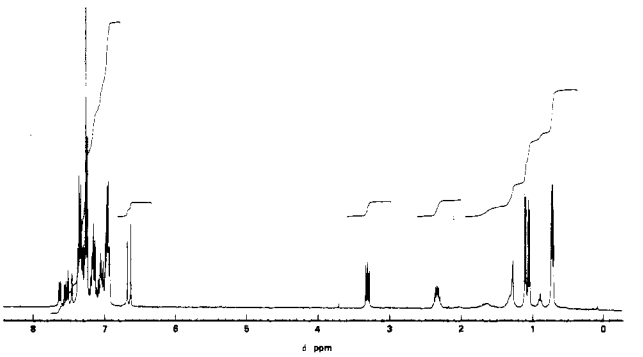
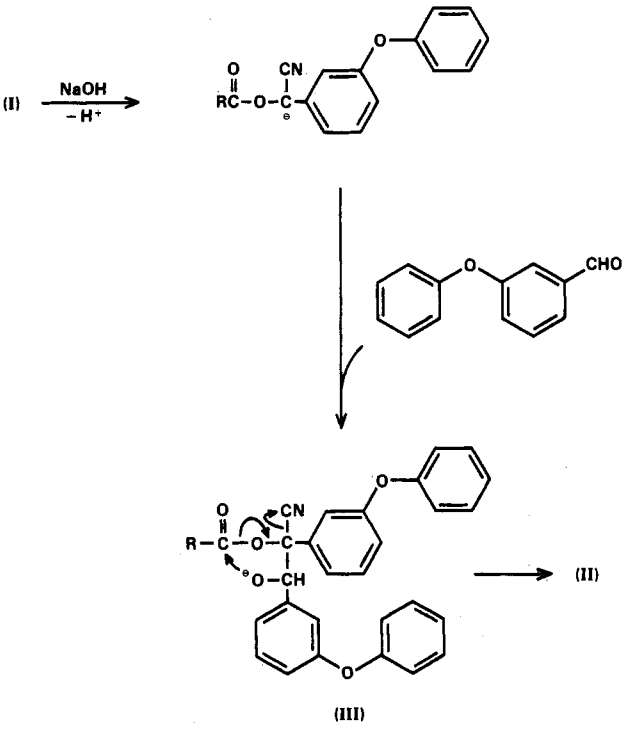


Figure 3. NMR spectrum of the mixture of diastereoisomers from the reaction of IA with 3-phenoxybenzaldehyde.

Scheme II



aldehydes. However, we believe that the occurrence of such a side reaction in the alkaline hydrolysis of pyrethroids has not been reported previously. Unfortunately, both benzoin esters derived from IA and IB are too photochemically unstable to be of any pesticide value.

Registry No. IA, 66230-04-4; IB (isomer I), 66290-21-9; IB (isomer II), 67375-30-8; 4-chloro-α-(1-methylethyl)benzeneacetic acid, 55332-38-2; 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, 59042-49-8; 3-phenoxybenzaldehyde, 39515-51-0.

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