Structure–Reactivity Relationships in the Hydrolytic Degradation of Propham, Chlorpropham, Swep, and Related Carbamates

Michel Bergon and Jean-Pierre Calmon*

The alkaline hydrolysis of propham, chlorpropham, and swep to carbanilic acids was investigated for sodium hydroxide concentrations ranging from 0.01 to 4.0 N. The dependence of the observed pseudo-first-order rate constants on the hydroxide ion concentration was in agreement with the rate laws of the two reaction mechanisms—E1cB and $B_{Ac}2$—that can be involved in the hydrolysis of carbamates. The values of the ionization constants of propham ($pK_a = 15.0$), chlorpropham ($pK_a = 14.45$), and swep ($pK_a = 13.9$) account for their behavior in aqueous media. The Hammett ρ value of 0.98 obtained for the hydrolysis of a series of isopropyl carbanilates, the activation entropy of swep and the changeover in reaction mechanism, from E1cB to $B_{Ac}2$, observed in the hydrolysis of alkyl and aryl 3,4-dichlorocarbanilates are decisive arguments supporting the involvement of a $B_{Ac}2$ reaction scheme in the hydrolysis of propham, chlorpropham, and swep. The formation of phenyl isocyanate during the degradation of these herbicidal carbanilates can therefore be ruled out.

Substituted carbamic acid esters, or carbamates, R′NHCOOR, are widely used in agriculture as pesticides (Melnikov, 1971). Carbanilic acid aliphatic esters, such as isopropyl carbanilate (propham, IPC) and isopropyl 3-chlorocarbanilate (chlorpropham, CIPC), are selective pre- and postemergence herbicides used for the control of annual grasses and broadleaf species in a variety of tolerant crops. 3,4-Dichlorocarbanilic acid metyl ester (swep) is applied on rice crops in Japan (Kuwatsuka, 1972). Owing to their antimitotic activity (Marth and Schultz, 1952), propham and chlorpropham are widely used, particularly in France (Bailly and Dubois, 1981), as sprout inhibitors during the storage of potato tubers.

In soils, chlorpropham (Kaufman and Kearney, 1965; Kearney and Kaufman, 1965; Clark and Wright, 1970a), propham (Clark and Wright, 1970b; Kaufman and Blake, 1973), and swep (Bartha and Pramer, 1969; Kaufman and Blake, 1973) are converted into anilines, carbon dioxide, and alcohols by microorganisms. The 3-chloro- and 3,4-dichloroanilines formed then give rise to 3,3′-dichloro- and 3,3′,4,4′-tetrachloroazobenzenes, respectively (Bartha et al., 1968).

In plants, such as soybean (Still and Mansager, 1973a), alfalfa (Zurquiyah et al., 1976), and sugar beet and wheat (Burt and Corbin, 1978), the hydroxylation of propham at the 2- and 4-positions on the aromatic ring and the aliphatic chain is the major metabolic pathway. In animals, in addition to the hydroxylated derivatives, other metabolites (10–20%) are generated by the hydrolysis of the carbamate function (Paulson et al., 1972, 1973; Fang et al., 1974).

The metabolism of chlorpropham is analogous to that of propham. As a matter of fact, in plants, particularly in soybean, Still and Mansager (1973b) could give evidence for the hydroxylation of the aromatic ring or of the aliphatic chain. However, in the rat, 40% of the amount of chlorpropham administered orally or intraperitoneally is metabolized through hydrolysis of the carbamate function (Bobik et al., 1972; Fang et al., 1974).

The literature provides little information on the molecular fate of swep in plants and animals.

Aly and El-Dib (1971) determined the half-lives of pesticidal carbamates in distilled water and could show that their stability in natural waters depends on the pH

and temperature of the medium. The effect of the molecular structure of carbamates on their reactivity toward hydrolysis was characterized by a Brönsted relationship (Williams, 1973; Wolfe et al., 1978a). N-Monosubstituted carbamates, such as carbaryl, are readily hydrolyzed under the conditions commonly occurring in aquatic environments; the pK_a value of the alcohol corresponding to their ester group is lower than 12. However, isopropyl carbanilates, such as propham and chlorpropham, are much more stable, as shown by their half-lives at pH 9.0 and 27 °C: $t_{1/2} > 10^4$ days (Wolfe et al., 1978b); the pK_a value of the conjugate acid of the leaving group, i-PrO⁻, is ca. 16.

As these herbicides are little reactive, their alkaline hydrolysis was investigated so as to elucidate the reaction mechanism (Figure 1) which might involve the formation of an isocyanate intermediate (Hegarty and Frost, 1973; Douglas and Williams, 1975), as shown in the case of carbaryl (Vontor et al., 1972) and of O-(methylcarbamoyl) oximes (Mrlina and Calmon, 1980). Isopropyl esters, which are used as sprout inhibitors, can practically undergo alkaline hydrolysis during the chemical peeling of potato tubers in sodium hydroxide solutions (Martens et al., 1971).

Owing to their high reactivity toward water, transient isocyanate intermediates cannot be characterized directly within the reaction medium (Mohr, 1906). However, the kinetic investigation of the alkaline hydrolysis of the three pesticidal carbanilates considered was liable to provide information on the reaction pathway—E1cB or $B_{Ac}2$—actually involved. Moreover, a series of variously N-phenyl-substituted isopropyl carbanilates as well as a series of 3,4-dichlorocarbanilic acid alkyl and aryl esters were synthesized so as to determine the effect of the chemical structure on the rate of hydrolysis.

EXPERIMENTAL SECTION

Apparatus. A Unicam SP 1800 recording spectrophotometer, fitted with a SP1805 program controller and a thermostated multiple cell compartment, was used for all spectroscopic measurements. The pH measurements were carried out by using a Radiometer PHM 64 pH meter equipped with a Radiometer GK 2321 C electrode.

Synthesis of Carbanilates. *Isopropyl Esters.* A substituted phenyl isocyanate (0.05 mol) was reacted with isopropyl alcohol (0.05 mol) in anhydrous benzene (40 mL) in the presence of triethylamine (2 mL) used as a catalyst. The reaction mixture was refluxed for 0.5 h.

Isopropyl chloroformate (0.05 mol) was reacted with N-methylaniline (0.05 mol) in dichloromethane in the presence of triethylamine to yield isopropyl N-methyl-N-

$$XYC_6H_3NHCOOR \underset{k_{-a}}{\overset{K_a}{\rightleftharpoons}} XYC_6H_3\bar{N}\ COOR$$

ElcB

$$XYC_6H_3\ N = C = O + RO^-$$

$k_2OH^- \| k_{-2}$ $\downarrow k_1$

$B_{Ac}2$

OH
|
$XYC_6H_3NHC-OR \longrightarrow XYC_6H_3NHCOO^- + RO^-$
|
O^-

X = Y = H	R = iPr	propham
X = 3-Cl, Y = H	R = iPr	chlorpropham
X = 3-Cl, Y = 4-Cl	R = Me	swep
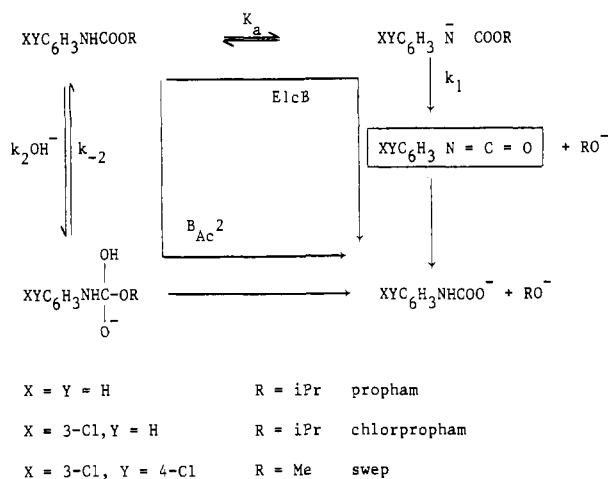
Figure 1. Mechanisms of alkaline hydrolysis of carbanilates.

Table I. Physicochemical Characteristics of Isopropyl Carbanilates $XC_6H_4N(R)COO$-*i*-Pr

X	R	mp, °C[a]	lit. mp, °C
m-NO$_2$	H	91–92	91[b]
m-Cl	H	40–41	41[b]
p-Cl	H	103	104[b]
H	H	89	89[b]
m-Me	H	37	39[c]
p-Me	H	54	52[b]
p-MeO	H	64	63[d]

| | | | elemental analysis | | | | |
| | | calcd | | | found | | | bp, °C |
X	R	C	H	N	C	H	N	(2 mmHg)
H	Me	68.37	7.82	7.29	69.08	7.83	7.46	80

[a] Recrystallized from hexane–chloroform. [b] Baskakov and Melnikov (1954). [c] Shulman and Griepentrog (1962). [d] Brunner and Wöhrl (1933).

phenylcarbamate after refluxing for 2 h. The carbamate, an oil, was then obtained after vacuum distillation.

The physical characteristics of the derivatives thus prepared are listed in Table I.

3,4-Dichlorocarbanilic Acid Esters. 3,4-Dichlorophenyl isocyanate (0.05 mol) was reacted with the corresponding alcohol or phenol (0.05 mol) in anhydrous benzene (40 mL) in the presence of catalytic amounts of triethylamine. The physical characteristics of these esters are listed in Table II.

The structure of all these carbanilates was corroborated by the detailed analysis of their NMR spectra.

Kinetic Measurements. *Substituted Phenyl 3,4-Dichlorocarbanilates.* The changes in concentration were followed spectrophotometrically by recording at appro-

priate wavelengths the changes in optical density corresponding to the disappearance of the substrate or to the appearance of the substituted carbanilate anion and/or of the substituted phenol. All reactions exhibited good first-order kinetics with respect to the substrate. The absorbance vs. time plots gave the pseudo-first-order rate constants graphically by using the experimental infinity value. The observed rate constants k_{obsd} were obtained by plotting log $(A_t - A_\infty)$ vs. time, where A_∞ and A_t are the absorbance readings at infinity and at time t, respectively: log $(A_t - A_\infty)$ = log $A_0 - (k_{obsd}/2.303)t$. Apparent second-order rate constants k_{OH} are the mean values calculated from $k_{obsd}/[OH^-]$ for four different hydroxide ion concentrations. Regression lines were obtained from a weighted least-squares program written for the Hewlett-Packard HP 97.

Isopropyl Carbanilates and Alkyl 3,4-Dichlorocarbanilates. In weakly alkaline media (pH <11), the UV spectra of alkyl carbanilates exhibit an intense absorption peak around 235 nm (ϵ ca. 15000). In alkaline media (0.005 N < [OH$^-$] < 1.0 N), the difference in absorbance between esters and carbanilic acids is very small and the reaction progress cannot be followed by recording directly the changes in optical density. The following procedure was then used: at definite time intervals, a 2-mL sample of an alkaline carbanilate solution was acidified with 1 mL of concentrated hydrochloric acid to yield anilinium ions after the instant decarboxylation of the carbanilic acid (Caplow, 1968; Johnson and Morrison, 1972). The changes in optical density of the acidified samples were measured at 235 nm, where only the carbanilate ester exhibits an absorption.

Over the pH range 7.5–9.5, the rate of the decarboxylation reaction of 3,4-dichlorocarbanilic acid is of the same order of magnitude as that of the formation of the phenolate ion from phenyl 3,4-dichlorocarbanilate. Two consecutive reactions are then involved:

$$A \xrightarrow{k'} B \xrightarrow{k} C$$
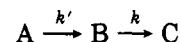
The procedure described above then allowed the rate constant k' for the formation of the phenolate ion to be determined.

As aryl 3,4-dichlorocarbanilates are water insoluble, the rate constants for the hydrolysis of alkyl and aryl 3,4-dichlorocarbanilates were measured in a 3:1 v/v water–dioxane mixture.

Solutions. The aqueous solutions were prepared by using deionized water which was then distilled over potassium permanganate and sodium hydroxide. Nitrogen was bubbled through the distilled water used for the preparation of the sodium hydroxide solutions.

pK_a Measurements. The UV spectra of propham, chlorpropham, and swep were recorded at 25 °C for various

Table II. Physicochemical Characteristics of Alkyl and Substituted Phenyl 3,4-Dichlorocarbanilates $3,4$-$Cl_2C_6H_3NHCOOR$

| | | | elemental analyses | | | | | | | |
| | | | calcd | | | | found | | | |
R	mp, °C[a]	lit. mp, °C	C	H	N	Cl	C	H	N	Cl
p-NO$_2$C$_6$H$_4$	209		47.73	2.46	8.56	21.68	48.10	2.41	8.39	21.75
p-AcC$_6$H$_4$	193		55.58	3.42	4.32	21.87	55.68	3.38	4.20	21.83
m-AcC$_6$H$_4$	196	193[b]								
C$_6$H$_5$	137		55.35	3.22	4.96	25.13	55.22	2.98	5.17	26.19
CH$_2$CCl$_3$	131		32.04	1.79	4.15	52.54	32.22	1.77	4.05	52.59
CH$_2$CH$_2$OCH$_3$	58	57[c]								
CH$_3$	114	112[c]								
CH$_2$CH$_3$	59	73[c]	46.18	3.88	5.98	30.29	46.71	3.68	6.11	30.52

[a] Substituted phenyl carbanilates were recrystallized from dioxane and phenyl and alkyl carbanilates from hexane–chloroform. [b] Cottin and Mocotte (1964). [c] Beaver et al. (1963).
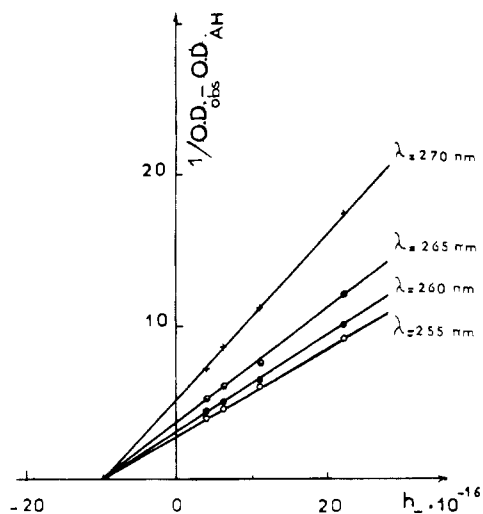
Figure 2. Plot of $1/(OD_{obsd} - OD_{AH})$ vs. h_- for the spectrophotometrical determination of the pK_a value of propham at 25 °C.

sodium hydroxide concentrations (0.1–6.0 M) corresponding to definite values (Coussemant et al., 1969) of the basicity function h_- (Hammett, 1940). As the completely ionized form could not be reached for each of these substrates, the data obtained from spectroscopic measurements were treated by the method developed by Maroni and Calmon (1964) and later adopted in the revised edition of Albert and Serjeant (1971): $1/(OD_{obsd} - OD_{AH})$ was plotted against h_- at various wavelengths. OD_{AH} and OD_{obsd} are the optical densities of the nonionized carbanilate (as determined in a borax solution of pH 9.18) and of the mixture of the nonionized carbanilate and its anion at a definite hydroxide ion concentration, respectively. Figure 2 shows the plot obtained for propham ($K_a = 10^{-15}$).

Thermodynamic Parameters of Activation. When the logarithms of the observed pseudo-first-order rate constants k_{obsd} were plotted vs. $1/T$, straight lines were observed, the slopes of which multiplied by $-2.303R$ gave the Arrhenius activation energy E_a. The entropy of activation ΔS^* was obtained from the equation $\log k_{obsd} = 0.43 \log (K/h) + \log T - E_a/(2.3RT) + \Delta S^*/(2.3R)$ where K and h are the Boltzman and Planck constants, respectively, and R is the gas constant.

RESULTS AND DISCUSSION

Alkaline Hydrolysis of Propham and Chlorpropham. *Effect of the Sodium Hydroxide Concentration.* The rates of hydrolysis were measured spectrophotometrically at 50 °C for various sodium hydroxide concentrations (0.01–3.0 M). Figure 3 shows the plots of the logarithms of the observed pseudo-first-order rate constants k_{obsd} against the hydroxide ion concentration for the two carbamates considered.

The straight lines of slope 1.07 and 1.00 obtained for propham and chlorpropham, respectively, are in agreement with the simplified expressions ($k_{obsd} = k_1K_a/a_H$ and $k_{obsd} = k_2$ [OH⁻] when $a_H \gg K_a$) of the rate laws corresponding to the E1cB and $B_{Ac}2$ reaction schemes, respectively:

$$k_{obsd} = k_1K_a/(K_a + a_H) \qquad (1)$$

$$k_{obsd} = k_2K_w/\gamma_{OH} - (K_a + a_H) \qquad (2)$$

The straight line of slope unity is followed by a plateau at higher pH values ($a_H \ll K_a$). The plateau could not be reached in the case of propham as it corresponds to [OH⁻] > 10 N. However, the plot obtained for chlorpropham tends to level off as the sodium hydroxide concentration exceeds 1.0 M. The shape of these profiles results from the high pK_a values of the derivatives investigated: 15.0
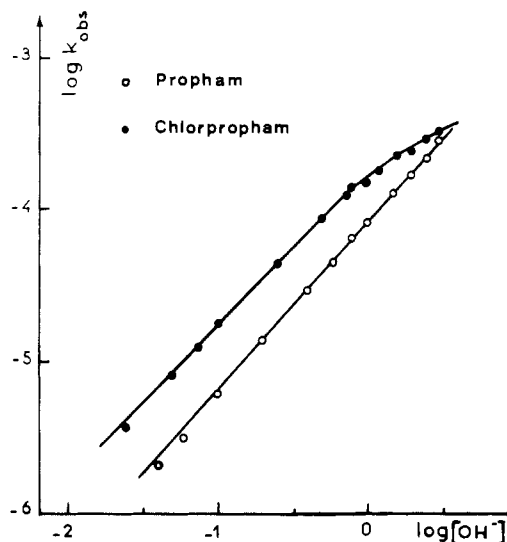
Figure 3. Plot of $\log k_{obsd}$ vs. $\log$ [OH⁻] for the hydrolysis of propham (open circles) and chlorpropham (closed circles) at 50 °C.

and 14.45 for propham and chlorpropham, respectively, at 25 °C.

Reaction Mechanism. Thermodynamic or kinetic parameters, such as the activation entropy or the deuterium oxide solvent isotope effect, may have values that are characteristic of an E1cB reaction mechanism when the rate constant is not composite. This is the case for the "plateau rates" as $k_{obsd} = k_1$ (Bergon and Calmon, 1976; Sartoré et al., 1977). Since the plateau could not be reached in the case of isopropyl esters, the above criteria could not be used.

The comparison of the rates of hydrolysis of propham and N-methylpropham was then considered. As the proton of the nitrogen atom of propham is substituted by a methyl group, the anion involved in the E1cB reaction scheme cannot be formed: the hydrolysis of N-methylpropham can then proceed only through the bimolecular $B_{Ac}2$ process. The bimolecular rate constants k_{OH} calculated from the pseudo-first-order rate constants k_{obsd} ($k_{OH} = k_{obsd}/$ [OH⁻]; 0.1 N < [OH⁻] < 1.0 N; 25 °C) were 8.12 × 10⁻⁶ and 7.72 × 10⁻⁷ L·mol⁻¹·s⁻¹ for propham and N-methylpropham, respectively. The former derivative is therefore 10-fold more reactive than the latter. Since a quite comparable difference in reactivity has already been reported for ethyl carbanilate and its N-methyl homologue (Williams, 1973), a competition between the E1cB and $B_{Ac}2$ reaction mechanisms might account for the data observed.

The Brönsted relationship between the logarithm of the bimolecular rate constant k_{OH} and the pK_a of the leaving group can be used to distinguish between E1cB and $B_{Ac}2$ mechanisms, as the value of the slope β of the Brönsted straight line is characteristic of the reaction mechanism involved: it is smaller than -1.0 for an E1cB scheme and greater than -0.5 for a $B_{Ac}2$ pathway (Williams, 1973; Bergon and Calmon, 1976; Sartoré et al., 1977).

However, as a result of the discrepant pK_a values of 2-propanol (15.5 < pK_a < 17.1) reported in the literature (Murto, 1964; Jencks and Regenstein, 1970; Cohen et al., 1971; Sauers et al., 1975), the Brönsted relationship, in the case of carbanilates and N-methylcarbanilates (Williams, 1973), could not include propham.

As the N-methylation and the Brönsted relationship did not afford an unambiguous characterization of the mechanism of hydrolysis of propham, this approach was not used for chlorpropham. As a matter of fact, the investigation of substituent effects proved to be more decisive.

Hydrolytic Degradation of Carbamic Acid Esters

J. Agric. Food Chem., Vol. 31, No. 4, 1983 **741**

Table III. Bimolecular Rate Constants k_{OH} for the Hydrolysis of Isopropyl Carbanilates $XC_6H_4NHCOO\text{-}i\text{-}Pr$ at 25 °C

X	$10^5 \times k_{OH}$, $L \cdot mol^{-1} s^{-1}$	correlation coeff, r	SD, s
$3\text{-}NO_2$	4.59	0.999	0.04
3-Cl	1.79	0.999	0.01
4-Cl	1.37	0.999	0.02
H	0.812	0.999	0.01
3-Me	0.739	0.998	0.02
4-Me	0.593	0.999	0.01
4-MeO	0.495	0.999	0.01
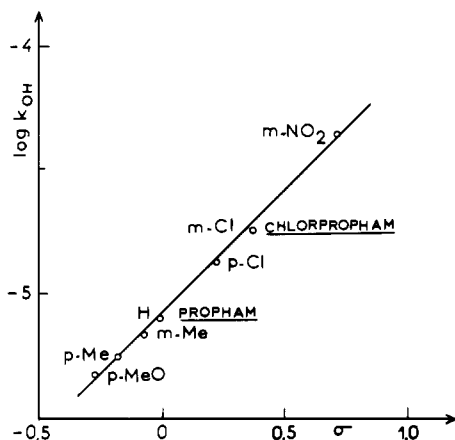
Figure 4. Hammett plot of log k_{OH} vs. σ for the hydrolysis of isopropyl carbanilates at 25 °C. [The datum points are surrounded by circles whose radius is equal to the standard deviation on log k_{OH} (±0.01 log unit)].

Effects of Substituents on the Alkaline Hydrolysis of a Series of Isopropyl Carbanilates: Hammett Relationship. N-Phenyl ring substituents of a series of isopropyl carbanilates could be expected to provide differing Hammett ρ values in the case of a changeover in reaction mechanism as the reactive sites involved are then different (Hammett, 1970). A further advantage of this structure–reactivity approach is that it does not call upon the pK_a value of 2-propanol.

The dependence of the observed pseudo-first-order rate constants k_{obsd} on the hydroxide ion concentration was in agreement with the simplified expressions of eq 1 and 2: $k_{obsd} = k_1 K_a/a_H$ and $k_{obsd} = k_2[OH^-]$, respectively. The bimolecular rate constants $k_{OH} = k_{obsd}/[OH^-]$ (Table III) fitted a Hammett relationship (Figure 4).

Irrespective of the nature of the substituent borne by the N-phenyl group, the datum points for isopropyl carbanilates are on a straight line whose equation is log k_{OH} = $0.98\sigma - 5.07$ ($r = 0.997$, $s = 0.03$). The Hammett ρ value of 0.98 is quite consistent with a $B_{Ac}2$ reaction mechanism where hydroxide ion attack at the carbonyl group is the rate-determining step. The sensitivity of such a reaction mechanism to substituent effects, when a nitrogen or oxygen hetero atom is intercalated between the carbonyl and aromatic groups, is usually reflected by a ρ value close to unity ($1.0 \leq \rho \leq 1.3$). Such is the case for the hydrolysis of two series of anilides $RCONR'C_6H_4X$ [$R = Me$, $R' = H$, ρ 1.00 (Bender and Thomas, 1961); $R = CF_3$, $R' = Me$, ρ 1.18 (Schowen and Kershner, 1971)]. For these anilides, the sequence between the reaction center and the aromatic ring, which is the site of the substitution, is the same as that of isopropyl carbanilates [$R = O\text{-}i\text{-}Pr$, $R' = H$]. The same remark holds for the hydrolysis of aryl acetates and aryl benzoates $RCOOC_6H_4X$ [$R = CH_3$, ρ 1.00 (Bruice and Mayahi, 1960); $R = C_6H_5$, ρ 1.27 (Kirsch et al., 1968)]. It is worth pointing out that for an E1cB reaction mechanism,
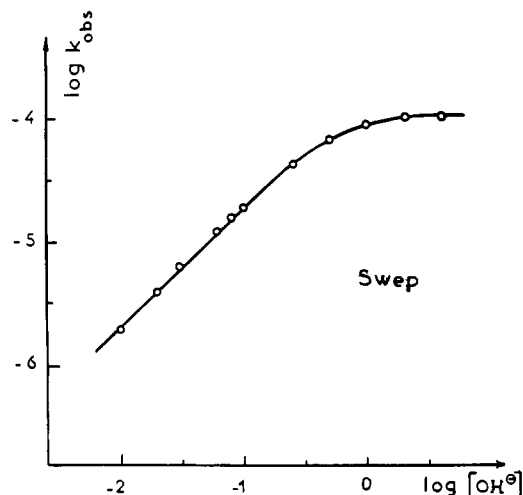

Figure 5. Plot of log k_{obsd} vs. log [OH^-] for the hydrolysis of swep at 25 °C.

Table IV. Temperature and Deuterium Oxide Solvent Isotope Effects on the Observed Pseudo-First-Order Rate Constants k_{obsd} for the Hydrolysis of Swep in 4.0 N NaOH

T, °C	$10^4 \times k_{obsd}$, s^{-1}	$10^4 \times k_{obsd}$, s^{-1}
25	1.04	1.04 (NaOH) 0.827 (NaOD)
35	2.47	
50	9.48	

$\Delta S^{\ddagger} = -20.5$ cal·deg^{-1}·mol^{-1}
$k_{obsd}(H_2O)/k_{obsd}(D_2O) = 1.25$

a much lower ρ value should be expected, as shown in the case of phenyl carbanilates $XC_6H_4NHCOOR$ [$R = C_6H_5$, ρ 0.64 (Hegarty and Frost, 1973)].

Alkaline Hydrolysis of Swep and 3,4-Dichlorocarbanilic Acid Esters. *Effect of the Sodium Hydroxide Concentration on the Hydrolysis of Swep.* The plot of log k_{obsd} vs. log [OH^-] (Figure 5) shows two distinct regions: a straight line of slope unity, followed by a plateau at higher sodium hydroxide concentrations. The shape of this profile is in agreement with the rate equations already mentioned for the E1cB and $B_{Ac}2$ reaction schemes.

The pK_a value of 13.9 obtained spectrophotometrically by the method of Maroni and Calmon (1964) is in excellent agreement with that determined kinetically from the intersecting point of the straight line of slope unity and of the plateau (Figure 5).

Mechanism of Hydrolysis. The reaction mechanism involved might be established by using criteria such as the entropy of activation and the deuterium oxide solvent isotope effect. These parameters were determined for sodium hydroxide concentrations corresponding to the plateau of the plot of log k_{obsd} vs. log [OH^-]. The data obtained for the effect of temperature on the observed pseudo-first-order rate constants and the values of the ratio $k_{obsd}(H_2O)/k_{obsd}(D_2O)$ are listed in Table IV.

The observed deuterium oxide solvent isotope effect of 1.25 is in good agreement with the calculated value of 1.15 obtained for a $B_{Ac}2$ reaction scheme. The value of -20.5 cal·deg^{-1}·mol^{-1} obtained for the entropy of activation cannot be accounted for by an E1cB reaction mechanism since the unimolecular decomposition of the anion should correspond to a positive activation entropy. On the contrary, in the case of a $B_{Ac}2$ mechanism, when k_{obsd} = $k_2 K_w/(\gamma_{OH^-}K_a)$, the entropy of activation is negative. The value observed for swep is of the same order of magnitude as that found for hydroxide ion addition to the carbonyl

Table V.   Bimolecular Rate Constants k_{OH} for the
Hydrolysis of Aryl and Alkyl 3,4-Dichlorocarbanilates at
25 °C in 3:1 v/v Water-Dioxane and pK_a Values
of the Leaving Group ROH

R	pK_a (R_{OH})	k_{OH}, L·mol^{-1}·s^{-1}	correlation coeff, r	SD, s
p-NO$_2$C$_6$H$_4$	7.15[a]	3.29 × 10^6	0.999	0.03
p-AcC$_6$H$_4$	8.05[a]	9.91 × 10^4	0.999	0.01
m-AcC$_6$H$_4$	9.19[a]	2.48 × 10^3	0.999	0.02
C$_6$H$_5$	9.86[b]	0.816 × 10^2	0.999	0.01
CCl$_3$CH$_2$	12.24[c]	3.67 × 10^{-2}	0.998	0.09
CH$_3$OCH$_2$CH$_2$	14.82[c]	6.520 × 10^{-5}	0.999	0.10
CH$_3$	15.09[d]	6.530 × 10^{-5}	0.998	0.27
CH$_3$CH$_2$	16.00[c]	2.990 × 10^{-5}	0.998	0.09

[a] Barlin and Perrin (1966).   [b] Jencks and Gilchrist
(1968).   [c] Ballinger and Long (1960).   [d] Murto (1964).

group of an ester (Kirby, 1973). Furthermore, a $\Delta S^{\ast}$ value
of -28 cal·deg^{-1}·mol^{-1} was determined from the values of
the bimolecular rate constants k_{OH} at 25 and 50 °C, for
sodium hydroxide concentrations corresponding to k_{obsd}
$= k_2[OH^-]$ in the case of a B$_{Ac}$2 pathway ($k_{OH_{25}°C}$ = 2.03
× 10^{-4} L·mol^{-1}·s^{-1} and $k_{OH_{50}°C}$ = 1.88 × 10^{-3} L·mol^{-1}·s^{-1}).

*Effect of the Leaving Group on the Alkaline Hydrolysis
of 3,4-Dichlorocarbanilates: Brönsted Relationship.* The
above arguments are for a B$_{Ac}$2 reaction scheme could be
further corroborated by the Brönsted relationship between
the logarithm of the bimolecular rate constant k_{OH} and the
pK_a of the leaving group of a series of aryl and alkyl 3,4-
dichlorocarbanilates.

The linear increase of the pseudo-first-order rate con-
stants with the hydroxide ion concentration is in agreement
with the simplified forms of eq 1 and 2. The bimolecular
rate constants k_{OH} listed in Table V were calculated from
$k_{OH} = k_{obsd}\gamma_{OH}\alpha_H/K_w$ with K_w = 1.00 × 10^{-15}, for a 3:1 v/v
water-dioxane mixture (Harned and Fallon, 1939). The
value of γ_{OH^-} was determined from the pH readings of
0.001-0.01 M sodium hydroxide solutions in a 3:1 v/v
water-dioxane mixture; γ_{OH^-} = 0.31.

The decrease in the rate of hydrolysis of swep in the
water-dioxane mixtures is of the same order of magnitude
as that observed for phenyl carbanilate (E1cB scheme) or
p-nitrophenyl N-methyl-N-(p-nitrophenyl)carbamate
(B$_{Ac}$2 scheme) under the same experimental conditions.
It is therefore to be pointed out that the reaction mecha-
nism is not affected by solvent effects (Hegarty and Frost,
1973).

The Brönsted plot of log k_{OH} vs. pK_a is shown in Figure
6.   The datum points for aryl and 2,2,2-trichloroethyl
3,4-dichlorocarbanilates are on a straight line whose
equation is

$$\log k_{OH} = -1.56 \ pK_a + 17.66 \ (r = 0.998, s = 0.05) \quad (3)$$

whereas the points obtained for aliphatic 3,4-dichloro-
carbanilates characterized by $pK_{a_{ROH}}$ > 14 are on another
straight line:

$$\log k_{OH} = -0.31 \ pK_a + 0.43 \ (r = 0.975, s = 0.06) \quad (4)$$

The intersecting point of these two straight lines corre-
sponds to a pK_a of ca. 13.5.

The marked difference in the Brönsted β values corre-
sponding to eq 3 and 4 suggests the occurrence of a
changeover in reaction mechanism, from E1cB to B$_{Ac}$2. As
a matter of fact, the β values reported in the literature for
the E1cB hydrolysis of various carbonyl derivatives, where
the elimination of RO$^-$ from the conjugate base of the
substrate is the rate-determining step, are smaller than -1.0
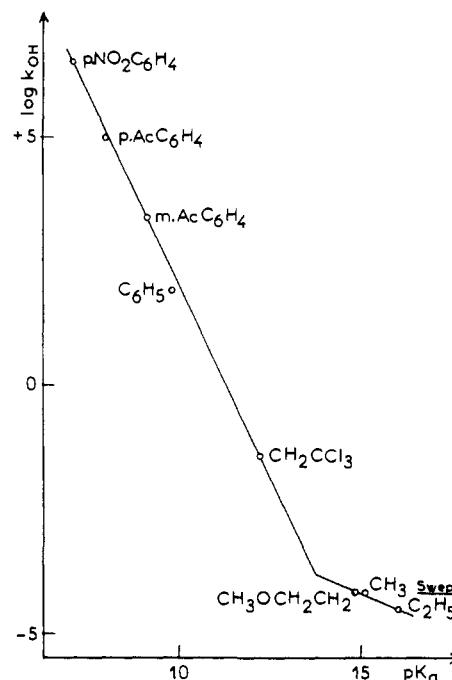(Table VI).

Figure 6. Brönsted plot of log k_{OH} vs. pK_a of leaving group for
the hydrolysis of alkyl and aryl 3,4-dichlorocarbanilates at 25 °C.

Table VI.   Brönsted Leaving Group Sensitivities β for
Various Carbonyl Species ($k_{OH} = k_1 K_a/K_w$)

conjugate base	β
N$^-$HCOOAr[a]	-1.15
CH$_3$N$^-$COOAr[a]	-1.10
C$_6$H$_5$N$^-$COOR[b]	-1.15
CH$_3$COC$^-$HCOSR[c]	-1.38
C$_6$H$_5$N$^-$CSOAr[d]	-1.35
CH$_3$CON$^-$COOAr[e]	-1.32

[a] Al-Rawi and Williams (1977).   [b] Williams (1973).
[c] Douglas and Yaggi (1980).   [d] Sartoré et al. (1977).
[e] Bergon and Calmon (1976).

Besides, the β value of -0.31 observed for aliphatic
3,4-dichlorocarbanilates is in good agreement with a B$_{Ac}$2
reaction scheme where the rate-determining step is hy-
droxide ion addition to the carbonyl group of the carba-
mate function. Comparable β values ($\beta > -0.5$) have been
reported in the literature for the B$_{Ac}$2 hydrolysis of ali-
phatic N-acetylcarbamates ($\beta = -0.23$; Bergon and Calmon,
1976), O-aryl N-methyl-N-phenylthiocarbamates ($\beta =$
-0.47; Sartoré et al., 1977), and p-nitrophenyl, phenyl, and
ethyl N-methyl-N-phenylcarbamates ($\beta = -0.25$; Williams,
1973).

This changeover in reaction mechanism, from E1cB to
B$_{Ac}$2, as the pK_a value of the leaving group of 3,4-di-
chlorocarbanilates reaches 13.5, is consistent with the data
of Williams (1973), who could show that aryl and alkyl
carbanilates hydrolyze via an E1cB pathway, and with
those of Hegarty and Frost (1973), who gave evidence for
a changeover in reaction mechanism from E1cB to B$_{Ac}$2
for aryl and alkyl N-(4-nitrophenyl)carbamates as the pK_a
value of the leaving group is of ca. 12.5. As a matter of
fact, the occurrence of increasingly electron-withdrawing
substituents on the aromatic ring ($\sigma_{3,4-Cl_2}$ = 0.52, σ_{4-NO_2} =
0.778) brings about a decrease in the reactivity of the
carbamate anion as a result of its increased stabilization
(Al-Rawi and Williams, 1977). An E1cB reaction scheme
can then operate only in the case of esters possessing
"good" leaving groups, i.e., alcohols or phenols whose pK_a
value is smaller than 12.5 (p-nitrocarbanilic acid esters)
or 13.5 (3,4-dichlorocarbanilic acid esters).

Hydrolytic Degradation of Carbamic Acid Esters

J. Agric. Food Chem., Vol. 31, No. 4, 1983 743

Moreover, the decisive argument provided by the Brönsted relationship for a $B_{Ac}2$ reaction scheme in the case of swep is consistent with that obtained from the Hammett relationship for the hydrolysis of methyl carbanilates bearing electron-withdrawing substituents on the aromatic ring (Bergon and Calmon, 1981).

CONCLUSIONS

The bimolecular rate constants determined for the alkaline hydrolysis of propham ($k_{OH} = 8.12 \times 10^{-6}$ L·mol^{-1}·s^{-1}), chlorpropham ($k_{OH} = 1.79 \times 10^{-5}$ L·mol^{-1}·s^{-1}), and swep ($k_{OH} = 2.03 \times 10^{-4}$ L·mol^{-1}·s^{-1}) at 25 °C show the high stability of these derivatives, even at high pH values.

In alkaline media, the hydrolytic breakdown of propham, chlorpropham, and swep, first to carbanilic acids and then to anilines, proceeds via a $B_{Ac}2$ reaction mechanism. Aryl isocyanate formation can therefore be ruled out, contrary to what is observed in the case of carbaryl (Vontor et al., 1972) and O-(methylcarbamoyl) oximes (Mrlina and Calmon, 1980) where methyl isocyanate is a reaction intermediate.

Under the alkaline conditions often met during the chemical peeling of potato tubers previously treated with antisprouting agents such as propham and chlorpropham, no toxicological hazard in relation to isocyanates is to be feared. Likewise, the occurrence of carbamoylation reactions involving the amino groups of some biological macromolecules (Lown and Chauhan, 1981) during the metabolism of propham, chlorpropham, and swep can be ruled out in animals as well as in plants.

ACKNOWLEDGMENT

We are grateful to D. R. Sayag for the translation of the manuscript.

Registry No. 3-NO$_2$C$_6$H$_4$NHCOO-i-Pr, 2610-62-0; 4-ClC$_6$H$_4$NHCOO-i-Pr, 2239-92-1; 3-MeC$_6$H$_4$NHCOO-i-Pr, 2610-63-1; 4-MeC$_6$H$_4$NHCOO-i-Pr, 36613-26-0; 4-MeOC$_6$H$_4$NHCOO-i-Pr, 85221-16-5; 3,4-Cl$_2$C$_6$H$_3$NHCOOC$_6$H$_4$-p-NO$_2$, 2204-76-4; 3,4-Cl$_2$C$_6$H$_3$NHCOOC$_6$H$_4$-p-Ac, 85221-17-6; 3,4-Cl$_2$C$_6$H$_3$NHCOOC$_6$H$_4$-m-Ac, 2689-50-1; 3,4-Cl$_2$C$_6$H$_3$NHCOOC$_6$H$_5$, 57148-27-3; 3,4-Cl$_2$C$_6$H$_3$NHCOOCH$_2$CCl$_3$, 85221-18-7; 3,4-Cl$_2$C$_6$H$_3$NHCOOCH$_2$CH$_2$OCH$_3$, 85221-19-8; 3,4-Cl$_2$C$_6$H$_3$NHCOOCH$_2$CH$_3$, 7159-94-6; propham, 122-42-9; chlorpropham, 101-21-3; swep, 1918-18-9.

LITERATURE CITED

Albert, A.; Serjeant, E. P. "The Determination of Ionization Constants", 2nd ed.; Chapman and Hall: London, 1971; Chapter 4, pp 44–64.
Al-Rawi, H.; Williams, A. J. Am. Chem. Soc. 1977, 99, 2671.
Aly, O. A.; El-Dib, M. A. Water Res. 1971, 5, 1191.
Bailly, R.; Dubois, G. "Index des produits phytosanitaires", 17th ed.; Acta: Paris, 1981; p 378.
Ballinger, P.; Long, F. A. J. Am. Chem. Soc. 1960, 82, 795.
Barlin, G. B.; Perrin, D. D. Q. Rev., Chem. Soc. 1966, 20, 75.
Bartha, R.; Linke, H. A. B.; Pramer, D. Science (Washington, D.C.) 1968, 161, 582.
Bartha, R.; Pramer, D. Bull. Environ. Contam. Toxicol. 1969, 4, 240.
Baskakov, Y. A.; Melnikov, N. N. Zh. Obshch. Khim. 1954, 24, 376.
Beaver, D. J.; Roman, D. P.; Stoffel, P. J. J. Med. Chem. 1963, 6, 501.
Bender, M. L.; Thomas, R. J. J. Am. Chem. Soc. 1961, 83, 4183.
Bergon, M.; Calmon, J. P. Bull. Soc. Chim. Fr. 1976, 797.
Bergon, M.; Calmon, J. P. Tetrahedron Lett. 1981, 22, 937.
Bobik, A.; Holder, G. M.; Ryan, A. J. Food Cosmet. Toxicol. 1972, 10, 163.
Bruice, T. C.; Mayahi, M. F. J. Am. Chem. Soc. 1960, 82, 3067.
Brunner, O.; Wöhrl, R. Monatsh. Chem. 1933, 63, 374.
Burt, M. E.; Corbin, F. T. Weed Sci. 1978, 26, 296.
Caplow, M. J. Am. Chem. Soc. 1968, 90, 6795.

Clark, C. G.; Wright, S. J. L. Soil Biol. Biochem. 1970a, 2, 19.
Clark, C. G.; Wright, S. J. L. Soil Biol. Biochem. 1970b, 2, 217.
Cohen, L. A.; Miller, H. K.; Peake, E. G.; Takahashi, S. J. Org. Chem. 1971, 36, 1205.
Cottin, C.; Mocotte, J. French Patent 1 381 253, Dec 11, 1964; Chem. Abstr. 1965, 63, 8259d.
Coussemant, F.; Hellin, M.; Torck, B. "Les fonctions d'acidité et leurs utilisations en catalyse acido-basique"; Gordon and Breach: New York, 1969; Vol. 3, p 52.
Douglas, K. T.; Williams, A. Chem. Rev. 1975, 75, 627.
Douglas, K. T.; Yaggi, N. F. J. Chem. Soc., Perkin Trans. 2 1980, 1037.
Fang, S. C.; Fallin, E.; Montgomery, M. L.; Freed, V. H. Pestic. Biochem. Physiol. 1974, 4, 1.
Hammett, L. P. "Physical Organic Chemistry"; McGraw-Hill: New York, 1940.
Hammett, L. P. "Physical Organic Chemistry, Reaction Rates Equilibria and Mechanism", 2nd ed.; McGraw-Hill: New York, 1970; Chapter 11, pp 355–357.
Harned, H. S.; Fallon, L. D. J. J. Am. Chem. Soc. 1939, 61, 2374.
Hegarty, A. F.; Frost, L. N. J. Chem. Soc., Perkin Trans. 2 1973, 1719.
Jencks, W. P.; Gilchrist, M. J. Am. Chem. Soc. 1968, 90, 2622.
Jencks, W. P.; Regenstein, J. "Handbook of Biochemistry", 2nd ed.; Sober, H. A., Ed.; Chemical Rubber Co.: Cleveland, OH, 1970; Section J.187.
Johnson, S. L.; Morrison, D. L. J. Am. Chem. Soc. 1972, 94, 1323.
Kaufman, D. D.; Blake, J. Soil Biol. Biochem. 1973, 5, 297.
Kaufman, D. D.; Kearney, P. C. Appl. Microbiol. 1965, 13, 443.
Kearney, P. C.; Kaufman, D. D. Science (Washington, D.C.) 1965, 147, 740.
Kirby, A. J. "Comprehensive Chemical Kinetics"; Bamford, C. H.; Tipper, C. F. H., Eds.; Elsevier: Amsterdam, 1973; Vol. 10, Chapter 2, p 57.
Kirsch, J. F.; Ciewell, W.; Simon, A. J. Org. Chem. 1968, 33, 127.
Kuwatsuka, S. "Environmental Toxicology Pesticides"; Matsumura, F.; Boush, G. M.; Misato, T., Eds.; Academic Press: New York and London, 1972; p 385.
Lown, J. W.; Chauhan, S. M. S. J. Med. Chem. 1981, 24, 270.
Maroni, P.; Calmon, J. P. Bull. Soc. Chim. Fr. 1964, 519.
Martens, P. H.; Nys, L.; Biston, R.; Fraselle, J. Bull. Rech. Agron. Gembloux 1971, 6, 127.
Marth, P. C.; Schultz, E. S. Am. Potato J. 1952, 29, 268.
Melnikov, N. N. "Chemistry of Pesticides"; Gunter, F. A.; Gunter, J. D., Eds.; Springer-Verlag: New York, 1971; pp 183–205.
Mohr, E. J. Prakt. Chem. 1906, 73, 177.
Mrlina, G.; Calmon, J. P. J. Agric. Food Chem. 1980, 28, 605.
Murto, J. Acta Chem. Scand. 1964, 18, 1043.
Paulson, G. D.; Doktor, M. M.; Jacobson, A. M.; Zaylskie, R. G. J. Agric. Food. Chem. 1972, 20, 867.
Paulson, G. D.; Jacobson, A. M.; Zaylskie, R. G.; Feil, V. J. J. Agric. Food. Chem. 1973, 21, 804.
Sartoré, G.; Bergon, M.; Calmon, J. P. J. Chem. Soc., Perkin Trans. 2 1977, 650.
Sauers, C. K.; Jencks, W. P.; Groh, S. J. Am. Chem. Soc. 1975, 97, 5546.
Schowen, R. L.; Kershner, L. D. J. Am. Chem. Soc. 1971, 93, 2014.
Shulman, S.; Griepentrog, J. A. Microchem. J. 1962, 6, 179.
Still, G. G.; Mansager, E. R. Pestic. Biochem. Physiol. 1973a, 3, 289.
Still, G. G.; Mansager, E. R. Pestic. Biochem. Physiol. 1973b, 3, 87.
Vontor, T.; Socha, J.; Vecera, M. Collect. Czech. Chem. Commun. 1972, 37, 2183.
Williams, A. J. Chem. Soc., Perkin Trans. 2 1973, 1244.
Wolfe, N. L.; Zepp, R. G.; Paris, D. F. Water Res. 1978a, 12, 561.
Wolfe, N. L.; Zepp, R. G.; Paris, D. F. Water Res. 1978b, 12, 565.
Zurquiyah, A. A.; Jordan, L. S.; Jolliffe, V. A. Pestic. Biochem. Physiol. 1976, 6, 35.