Kinetic Study and Mechanism Hydrolysis of 4-Bromo-3,5 dimethylphenyl N-methylcarbamate in Aqueous Media

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ABSTRACT: Degradation via hydrolysis is among the main transformation pathways and particularly for N-methylcarbamates. Carbamate pesticide hydrolysis is known to proceed through alkaline catalysis, with reaction of the hydroxide ion with the carbonyl function or with abstraction of hydrogen in the α position with respect to the carbonyl. This reaction leads to the formation of methylamine and corresponding phenol. In this respect, the reaction kinetics of 4-bromo-3,5-dimethylphenyl N-methylcarbamate (BDMC) hydrolysis have been investigated in alkaline solution using a spectrophotometric technique and reversed phase liquid chromatography. The kinetic constants were determined following a proposed pseudo–first-order kinetic model. The positive activation entropy $\Delta S^{\neq} = +35.73$ J mol^{-1} K^{-1} and the absence of general base catalysis indicated an unimolecular elimination conjugate base (E1cB) hydrolytic mechanism involving the formation of methyl isocyanate. This result was confirmed by the fact

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that BDMC fits well into brönsted and Hammett lines, obtained for a series of substituted N-methylcarbamate whose decomposition in aqueous media was established to follow an E1cB mechanism. Int J Chem Kinet 1–9, 2017

INTRODUCTION

Phenyl-*N*-methylcarbamate (PNMCs) pesticides are aryl esters of phenyl-*N*-methyl substituted carbamic acids [1]. The substituents on the phenyl ring can change the characteristic nature of the parent compound in hydrophobic, electronic, and hydrogen bonding and can thus affect the ability of complexation with acethylcholinesterase, a determining factor for its cholinesterase inhibition activity [2]. Most of PNMCs are degraded into their metabolites shortly after application. In alkaline media, PNMCs can be easily hydrolyzed to form methylamine and substituted phenols. The corresponding mechanism involves either an addition of OH^- into the carbonyl with a further elimination of the RO^- leaving group or an abstraction of the hydrogen of the methylcarbamate moiety again evolving with the elimination of the RO^- group. Consequently, we have undertaken in our laboratory a study of the determination of both the kinetic and mechanistic aspects of the hydrolysis reaction of carbaryl [3], carbofuran [4], methiocarb [5], bendiocarb [6], zectran [7], aminocarb [8], landrin [9], ethiofencarb [10], carzol [11], isoprocarb [12], and pirimicarb [13]. We showed that hydrolysis of PNMCs exhibited pseudo–first-order kinetics with respect to substrate in aqueous media. The positive activation entropy obtained and the fact that each *N*-methylcarbamate (NMC) fits well onto a brönsted and Hammett plots, obtained for a series of substituted *N*-methylcarbamate supports an unimolecular elimination conjugate base (E1cB) reaction scheme for the hydrolysis of PNMCs.

In this respect, this paper is an extension of such studies to the degradation scheme of 4-bromo-3,5dimethylphenyl *N*-methylcarbamate (BDMC) to yield 4-bromo-3,5-dimethylphenol in aqueous media. As part of our continuing interest in degradation of NMCs in aqueous matrices, kinetic and mechanistic aspects of the hydrolysis of BDMC were carried out. Our aims in this work were as follows: (1) to identify the major transformation product of BDMC by means of spectrophotometric UV and liquid chromatography, (2) to investigate the hydrolysis of BDMC in Milli-Q water under different pH and temperature values, and (3) to investigate the degradation of BDMC in environmental water.

EXPERIMENTAL

Materials

A SCINCO S-3100 spectrophotometer fitted with a thermostated multiple cell compartment was used for all spectroscopic measurements. The analysis and storage of data were carried out by means of software LabPro® Plus S W.

The liquid chromatography diode array detection (LC-DAD) system consists of a gradient model pump from Varian ProStar model 240, a rheodyne manual sample injector valve model 7725 i with a 20-μL loop. A model Varian ProStar 330 diode array detector was connected to a computer station. Separations were performed using a Symmetry C18, 150 × 4.6 mm i.d, 5-μm particulate size analytical column.

The mobile phase was acetonitrile–water (70:30, v/v). It was set at a flow rate of 1 mL min^{-1}. The measured wavelength was 200 nm.

Reagents and Solvents

BDMC and 4-bromo-3,5-dimethylphenol were obtained from Supelco (Saint-Quentin Fallavier, France). Methanol, acetonitrile, and water were of HPLC grade. Hydrochloric acid HCl (35–38%), Borax ($Na_2B_4O_7$, 10 H_2O), sodium hydroxide (NaOH), potassium dihydrogen phosphate (KH_2PO_4), sodium hydrogen phosphate (Na_2HPO_4), and potassium chloride (KCl) were purchased from Fluka (Saint-Quentin Fallavier, France).

Preparation of Solutions

The standard stock solution of BDMC of 1000 $\mu g \cdot mL^{-1}$ was prepared by dissolving 20 mg in 20 mL of methanol. The different aqueous solutions were prepared at different pH by the dilution of standard stock solution at a concentration of 10 $\mu g \cdot mL^{-1}$ in the appropriate buffer. The ionic strength (*I*) of these solutions was kept constant equal to the unity by addition of KCl.

Determination of the Rate Constant k_{obs} of the Hydrolysis Reaction of BDMC

Spectrophotometric Method. The kinetics of the hydrolysis reaction of the BDMC was followed by

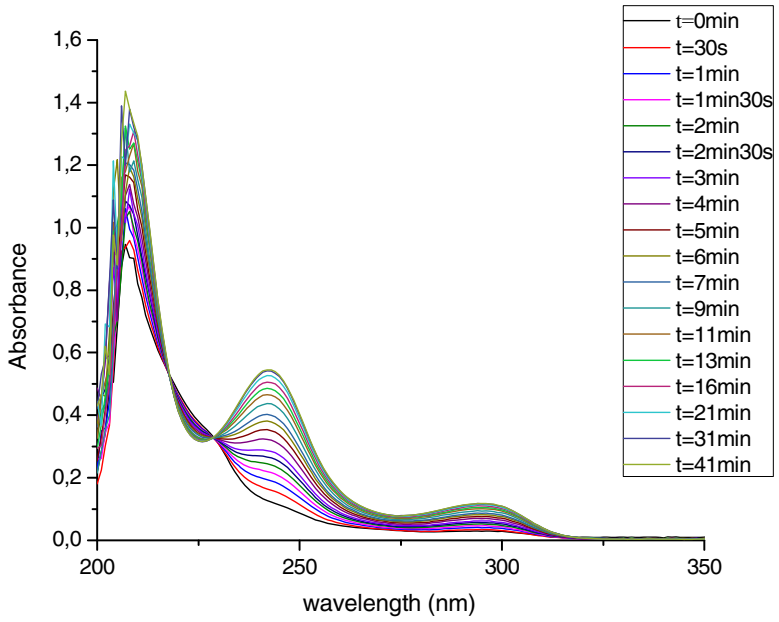


Figure 1 UV spectra versus time of the hydrolysis reaction of BDMC (10 μg·mL^{-1}) in phosphate buffer solution at pH 11.12, $T = 21$°C, and $I = 1.00$ M. [Color figure can be viewed at wileyonlinelibrary.com]

measuring the variation in absorbance versus time corresponding to the disappearance of the substrate or to the appearance of the hydrolysis product. The presence of two isobestic points at (λ = 218 nm and 229 nm) on the ultraviolet BDMC spectra recorded versus time indicates that there is no intermediate accumulation and that the reaction exhibited pseudo–first order with respect to the carbamate (Fig. 1). The observed rate constant k_{obs} was determined graphically from the slope of the following linear equation:

$$\ln(A_\infty - A_t) = -k_{obs}t + \ln(A_\infty - A_0) \qquad (1)$$

where A_0, A_∞, and A_t are, respectively, the absorbance at initial, infinity, and at time t.

Liquid Chromatographic Method. The recording of the chromatographic evolution versus time during the hydrolysis reaction of the BDMC is shown in Fig. 2. k_{obs} were obtained by plotting $\ln(A_\infty - A_t)$ versus time, where A_∞, and A_t are the peak area at infinity and at time t, respectively. (Eq. (1)).

Entropy Activation

The activation energy was determined from the slope of the straight line of the Arrhenius plot. The entropy activation $\Delta S^{\neq}$ was obtained from the following equation:

$$\Delta S^{\neq} = 2.3\,R\left(\log k_{obs} - \log\frac{e\,K_B}{h} - \log T\right) + \frac{E_a}{T} \qquad (2)$$

where h and K_B are the Planck and Boltzmann constants, respectively, and R is the gas constant $\log(\frac{e\,K_B}{h}) = 10.753$.

pKa Measurement

The pK_a of 4-bromo-3,5-dimethylphenol was determined experimentally by plotting:

$$\log\frac{A - A_{AH}}{A_{A^-} - A} = f\,(\text{pH})$$

where A_{A^-}, A_{AH}, and A are, respectively, the absorbances of the phenolate ion in 1 M NaOH, of the nonionized carbamate in 1 M HCl, and of the mixture of the two species in buffer solutions ranging from pH 8.7 to 11.5. The pKa value of 4-bromo-3,5-dimethylphenol was obtained from the intercept of the graph and is 9.95 ($T = 21$°C, $I = 1.00$, KCl).

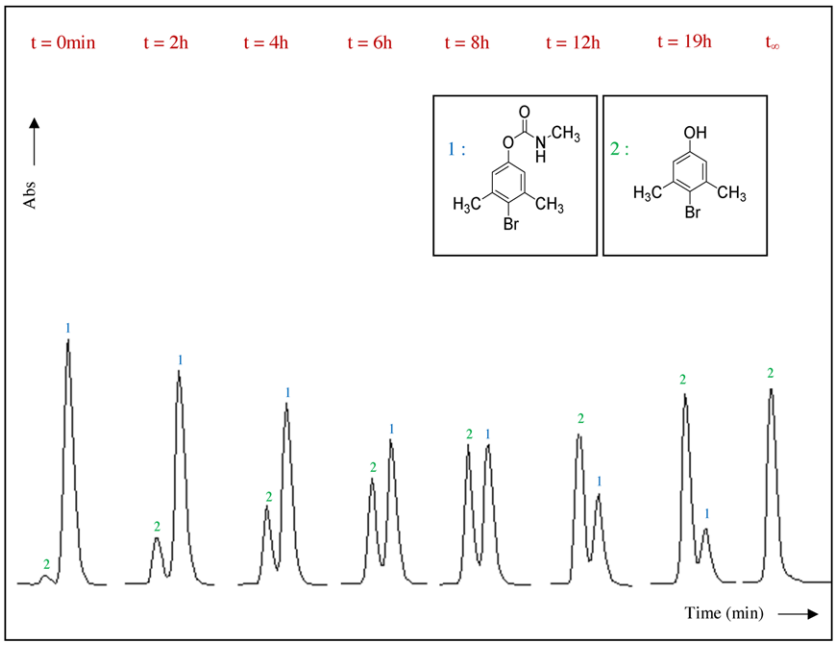


Figure 2 Chromatogram versus time of the hydrolysis of BDMC at pH 8.76, $T = 28°C$, and $I = 1$ M. [BDMC] = 10 μg·mL^{-1}; Column: INERTSIL ODS-4 C-18 (15 cm × 4.6 mm ID), dp: 5 μm; mobile phase: acetonitrile-water (70:30, v / v); Flow rate: 1 mL·min^{-1}; at λ = 200 nm; Inj: 20 μL. [Color figure can be viewed at wileyonlinelibrary.com]

RESULTS AND DISCUSSION

Determination of 4-Bromo-3,5-dimethylphenol as a Hydrolysis Product

The good superposition of the UV spectrum of the hydrolysis product (Fig. 3, spectrum c) with that of a 4-bromo-3,5-dimethylphenol (Fig. 3, spectrum b) confirmed that the BDMC hydrolyzes quantatively in 4-bromo-3,5-dimethylphenol. Furthermore, the chromatogram resulting from the hydrolysis reaction of the BDMC shows the presence of two peaks at the retention times $t_R = 4.05$ and 3.81 min corresponding, respectively, to the BDMC and its degradation product. The identification of the latter is carried out by comparing its retention time with an authentic sample (Fig. 4).

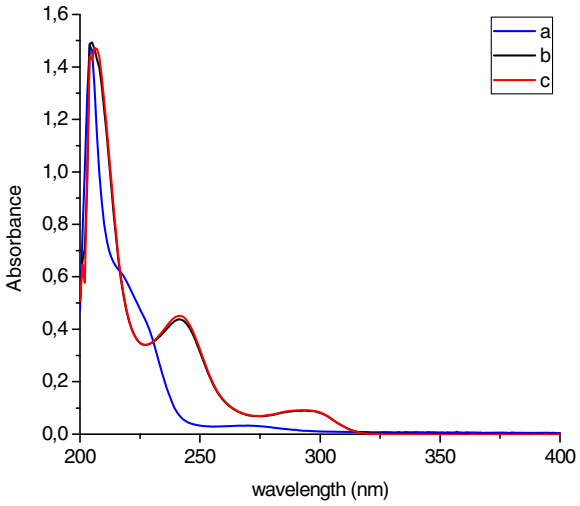


Figure 3 UV absorption spectra of BDMC (a) of 4-bromo-3,5-dimethylphenol (b) and of the hydrolysis product (c) at pH 10.33; $T = 21°C$ and $I = 1$M, [BDMC] = [4-bromo-3,5-dimethylphenol] = 10 μg·mL^{-1}. [Color figure can be viewed at wileyonlinelibrary.com]

Effect of pH

The pseudo–first-order rate constants of the hydrolysis reaction of BDMC in aqueous media at 21°C and for an ionic strength $I = 1.00$ M were determined in pH buffer solutions ranging from 7.6 to 12 by measuring the variation in absorbance versus time corresponding to the appearance of its degradation product at λ = 242 nm.

The logarithmic variation of the rate constant k_{obs} of the BDMC hydrolysis reaction as a function of pH is a straight line of slope one ($\log k_{obs} = 0.9014\,\text{pH} - 10.858$; $R^2 = 0.999$) (Fig. 5) of Eqs. (3) and (4). This

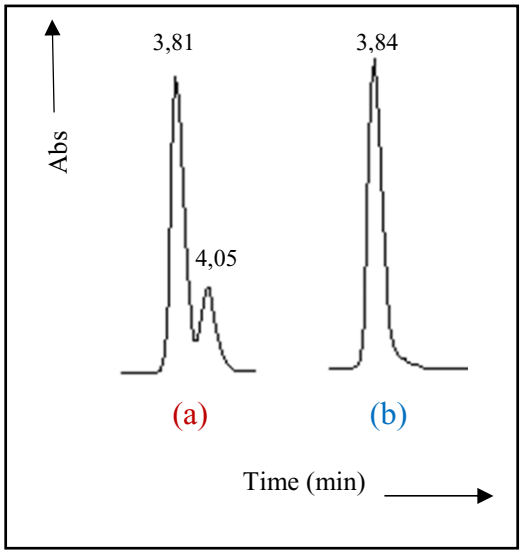


Figure 4 (a) Chromatogram of the BDMC during the hydrolysis reaction and (b) chromatogram of a 4-bromo-3,5-dimethylphenol standard solution. [Color figure can be viewed at wileyonlinelibrary.com]

slop value is in agreement with the limit forms obtained for $a_H \gg K_a$ and $a_H \ll K_a$.

$$k_{obs} = \frac{k_1 K_a}{a_H} \tag{3}$$

and

$$k_{obs} = k_2 \left[OH^-\right] \tag{4}$$

These equations corresponding respectively to the two mechanisms E1cB and a bimolecular addition conjugated base ($B_{Ac}2$) proposed for the hydrolysis reaction of the BDMC (Scheme 1) [14,15]. Both mechanisms E1cB and $B_{Ac}2$ differ mainly by the formation of a methyl isocyanate intermediate. The detection of this intermediate in the reaction medium is very difficult because of the extreme fugacity of this compound. In fact, the methyl isocyanate reacts rapidly with the hydroxyl ion to form *N*-methylcarbamic acid, which, by decarboxylation, leads to methylamine [16].

Possibility of Mechanism E2: Research for General Base Catalysis

A bimolecular elimination mechanism E2 may be proposed for the hydrolysis reaction of BDMC. It is in accordance with the formation of methylisocyanate (Scheme 2). Bender and Homer [17] suggested this mechanism for the hydrolysis of *p*-nitrophenyl-*N*-methylcarbamate in phosphate and imidazole buffer solutions. It involves a slow proton transfer that should be translated by a general base catalysis. The influence of the phosphate buffer concentration at pH 11.12 and $T = 21°C$ on the rate of BDMC hydrolysis was carried out (Table I). According to the experimental result, we noted that the observed rate constants of BDMC hydrolysis remain constant; so there is no general base catalysis, and the E2 mechanism is rejected.

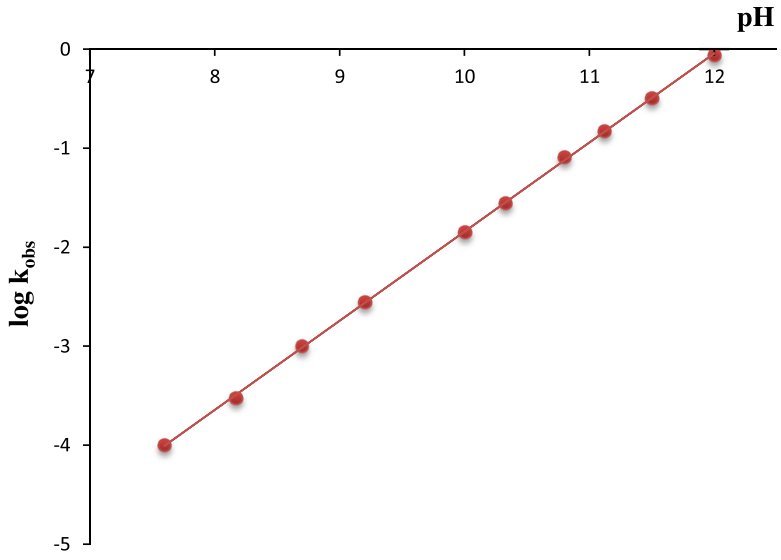
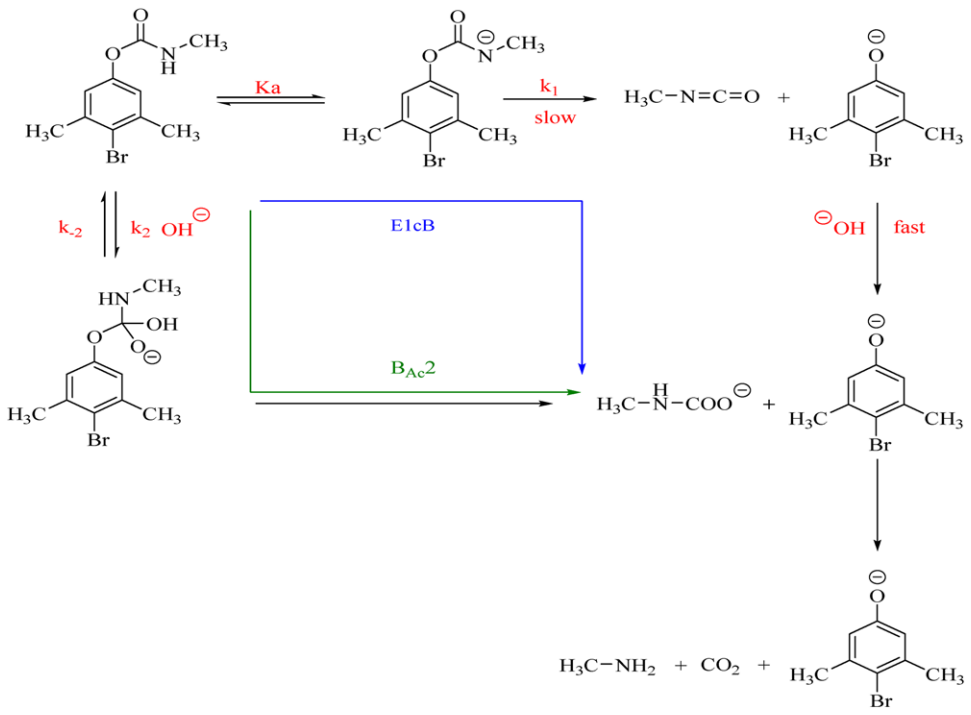
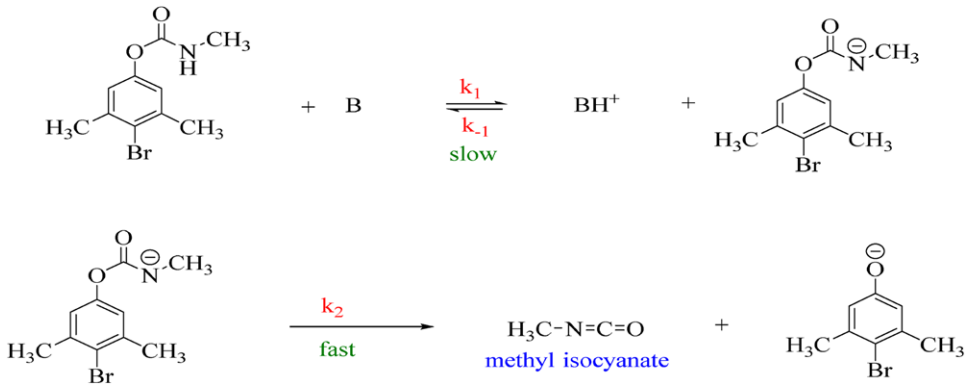


Figure 5 Logarithmic variation of the observed rate constant k_{obs} of the hydrolysis reaction of BDMC versus pH at 21°C. [Color figure can be viewed at wileyonlinelibrary.com]



Scheme 1 Hydrolysis of the carbamate studied according to two possible mechanisms E1cB and BAc2.



Scheme 2 A bimolecular elimination mechanism E2 for the BDMC hydrolysis reaction.

Table I Rate Constants of BDMC Hydrolysis at Different Phosphate Buffer Concentrations (pH 11.12) at 21°C

$[HPO_4^{2-}]$ ($\times 10^{-2}$ mol·L^{-1})	1	0.75	0,5	0.35	0.25
k_{obs} (min^{-1})	0.149	0.152	0.158	0.149	0.154

Effect of Temperature

Equations (3) and (4) are equivalent, so we cannot differentiate between the two mechanisms [18]. According to the data available in the literature, the activation entropy can be an argument in favor of one or the other E1cB and $B_{Ac}2$ mechanisms [19]. Indeed, the positive values of activation entropy corresponds to the mechanism E1cB ($\Delta S^{\neq} > 0$) whereas the negative values present a $B_{Ac}2$ mechanism ($\Delta S^{\neq} < 0$) [20]. Therefore to determine $\Delta S^{\neq}$, we measured the BDMC hydrolysis rate constants at temperatures between 21 and 45°C in a borax buffer solution of pH 10,33 and an ionic strength $I = 1.00$ M. The value of the activation entropy variation $\Delta S^{\neq} = +35.73$ J mol^{-1} K^{-1} is deduced from that of the activation energy $E_a = 93.48$ KJ mol^{-1}, calculated from the slope of the linear of equation

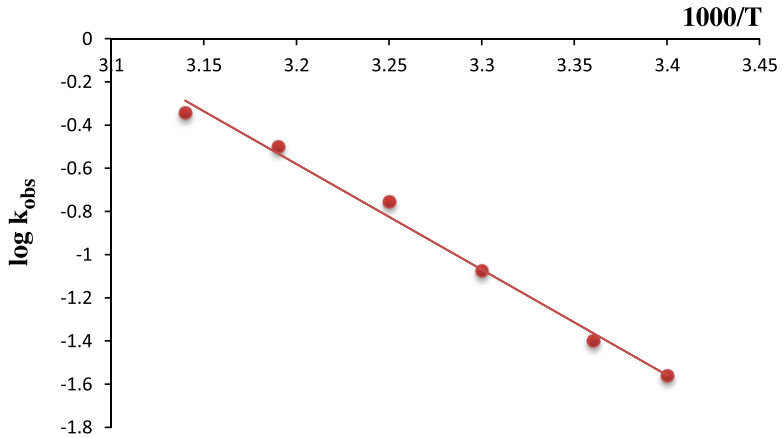


Figure 6 Logarithmic variation of the experimental rate constant k_{obs} versus the temperature for the BDMC hydrolysis. [Color figure can be viewed at wileyonlinelibrary.com]

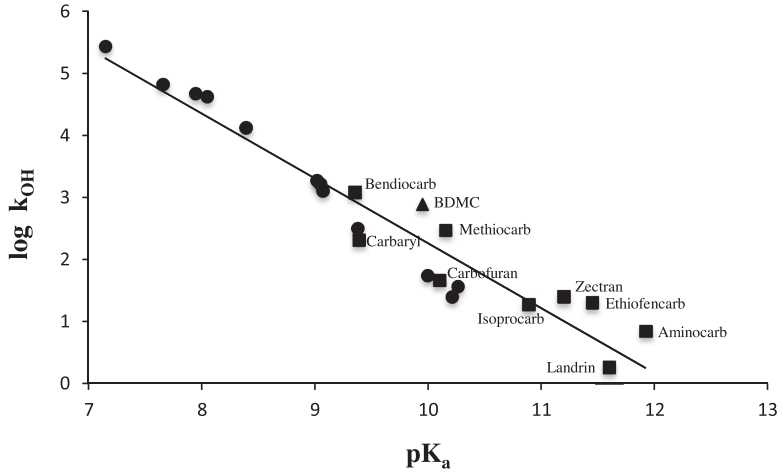


Figure 7 Brönsted plot of log k_{OH} versus pK_a of the leaving group for the hydrolysis of phenyl *N*-phenylcarbamates (•) and phenyl *N*-methylcarbamates (■). BDMC (▲).

$\log k_{obs} = -4.888 \times 1000/T + 15.062$ ($R^2 = 0.999$) (Fig. 6). The positive value of the activation entropy is in agreement with the mechanism E1cB. Comparable values were obtained for the hydrolysis reaction of a series of *N*-methylcarbamates studied in our laboratory: carbaryl [3], carbofuran [4], methiocarb [5], bendiorab [6], zectran [7], aminocarb [8], landrin [9], ethiofencarb [10], carzol [11], and isoprocarb [12].

The Brönsted line $\log k_{OH} = \beta\, pK_a + cte$, which relates the logarithm of the bimolecular rate constant to the pK_a of the leaving group, can be used to elucidate the mechanism of the BDMC hydrolysis. Indeed the slope β of this line is characteristic either of a mechanism E1cB (when $\beta < -0.1$) or of a mechanism BAc2 ($\beta > -0.5$). Williams studied the effect of substituents on the hydrolysis rate constants of the E1cB type of a series of phenyl *N*-phenylcarbamate. He pointed out a linear relationship $\log k_{OH} = -1.34\, pK_a + 15.2$ [21]. The slope of this line is characteristic of the mechanism E1cB.

The point corresponding to BDMC with the coordinate ($pK_a = 9.95$; $\log k_{OH} = 2.89$) was well introduced into the graph $\log k_{OH} = f(pK_a)$ (Fig. 7). It confirms that the BDMC degrades according to the E1cB mechanism. The logarithmic value of the bimolecular hydrolysis rate constant $\log k_{OH} = 2.89$ relative to the BDMC was determined from the ordinate at the origin of the line of equation $\log k_{obs} = f(pH)$.

Hammett Relationship

The Hammett relationship $\log k_{OH} = 2.865\,\sigma^- + 2.04$ established by Williams for the hydrolysis of a series of phenyl-*N*-phenylcarbamates is in favor of an E1cB

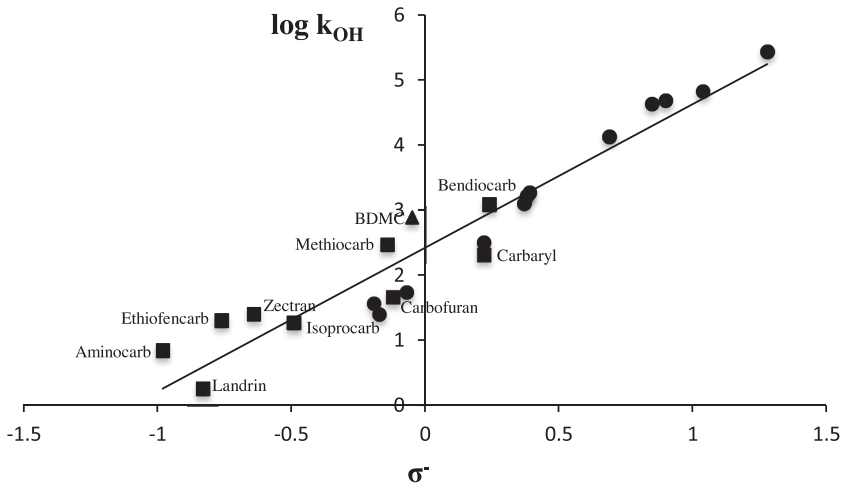


Figure 8 Hammett plot of log k_{OH} of hydrolysis of phenyl *N*-phenylcarbamates (•) and phenyl *N*-methylcarbamates (■) and Hammett σ- constants. BDMC (▲).

Table II Rate Constants of BDMC Hydrolysis Reaction in Surface Waters at pH 7.3 and Temperature 28°C

Samples	Oued Medjerda	STEP El Hancha (Sfax)	Barrage Aroussia	Eau Milli-Q
k_{obs} 10^4 (min^{-1})	0.2	0.6	0.2	1[a]

[a]pH 7.6; $T = 21$°C.

mechanism [21]. The experimental point corresponding to BDMC ($\sigma^- = -0.05$; log $k_{OH} = 2.89$) is positioned on the Hammett line (Fig. 8). The electronic parameter $\sigma^- = -0.05$ of the leaving group 4-bromo-3,5-dimethylphenol was calculated from the equation $-pK_a = 2.11\,\sigma - 9.85$ [22].

APPLICATION

The potential of the method for the hydrolysis of BDMC in surface water samples has been demonstrated. Samples of tap and surface water from different sampling sites (river, dam, and STEP) all over Tunisia were collected. The values of the observed rate constant of this reaction are reported in Table II. According to the found experimental results, we noted that the rate constant is greater in a Milli-Q water sample than in surface waters. This could be due to the presence of organic matter, which slows the rate of hydrolysis due to solute–organic interactions.

CONCLUSION

In this work, we presented the kinetic study and the hydrolysis mechanism in aqueous media of BDMC. This study was carried out using UV spectrophotometry and high-performance liquid chromatography with reverse phase polarity. The identification of 4-bromo-3,5-dimethylphenol as a degradation product shows the high reactivity of the carbamate function in aqueous medium. The hydrolysis reaction is pseudo–first order, and the rate constant k_{obs} calculated at pH 7.6 is equal to 0.01×10^{-2} min^{-1}. The positive activation entropy ($\Delta S^{\neq} = +35.73$ J mol^{-1} K^{-1}) and the absence of general base catalysis are in favor of an E1cB elimination. This elimination process is confirmed by the position of the experimental points, with coordinates ($pK_a = 9.95$; log $K_{OH} = 2.89$) and ($\sigma^- = -0.05$; log $K_{OH} = 2.89$), respectively, on the Brönsted and Hammett plots proposed by Williams for the hydrolysis of phenyl *N*-phenylcarbamates whose degradation proceeds according to the unimolecular process E1cB.

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