Kinetics of the Alkaline Hydrolysis of several Alkyl Phenylcarbazates

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The kinetics in 25% (v/v) dioxane–water of the alkaline hydrolysis, followed by UV spectrometry, of several alkyl phenylcarbazates (Ar–NH–NHCOOR, with Ar = phenyl, 4-chlorophenyl, 4-fluorophenyl, 3,4-dichlorophenyl and R = methyl, ethyl, propyl, chloroethyl, trichloroethyl) are discussed. The pK_a of trichloroethyl phenylcarbazate is 14.12 at 25 °C. The pH profiles, the activation entropy of −40 cal mol^{-1} K^{-1}, the kinetic solvent isotope effect, k_{OH^-}/k_{OD^-}, of 3.45, the general-base catalysis and the effect of the leaving group and of the substituent on the aromatic ring are in agreement with the involvement of a $B_{Ac}2$ reaction scheme.

Alkyl *N*-phenylcarbazates have a carbamic group in their structure. They belong to a class of pesticides called carbazates which are well known for their weed-killing[1] and fungicidal properties.[2] During investigations related to the biological utilization of these molecules, we examined their stability in aqueous media. In alkaline solution, carbazates are hydrolysed on their ester group with production of the corresponding phenylhydrazine, alcohol and carbon dioxide.

Experimental

Equipment.—Absorption measurements were carried out with a Varian Cary 210 spectrophotometer provided with a cell compartment which was thermally controlled to ±0.1 °C by means of circulating water. The ^1H NMR spectra were obtained on a Bruker 80 MHz apparatus. The pH was measured with a Radiometer PHM64 pH-meter equipped with a Radiometer GK 2401B electrode and constant temperature was maintained with circulating water. The IR analyses were carried out on a Perkin-Elmer 983 apparatus. The elementary analyses were performed at the CNRS using micro-analytical methods.

Reagents.—*Synthesis of alkyl* N-*phenylcarbazates.* Alkyl *N*-phenylcarbazates were prepared by addition of an alkyl chloroformate to phenylhydrazine in the presence of pyridine.[2]

Preparation of alkaline solutions. Sodium hydroxide solutions were prepared with deionized water and distilled after addition of potassium permanganate and sodium hydroxide. Nitrogen was subsequently bubbled through the water to prevent carbonation. The ionic strength of sodium hydroxide solutions (< 1 mol dm^{-3}) was kept constant and equal to 1 by addition of KCl.

Method.—The progress of the reaction was monitored by recording the UV spectra at various time intervals. An isosbestic point at 265 nm was found, which demonstrated that no intermediate products accumulated. The reaction was first order with respect to the substrate. A biphasic reaction can be observed, an increase of this absorption with time for the hydrolysis reaction followed by a slow decrease corresponding to the decarboxylation of the phenylhydrazine carboxylate. Absorption measurements were carried out at 275 nm for the determination of the rate constants, k_{obs}, from the relation $\ln(A_\infty - A_t) = k_{obs}t$, where A_∞ and A_t represent, respectively, the final absorption and the absorption at time *t*. When this reaction is rapid, A_∞ is constant and can be measured directly. For the slow reactions, A_∞ is extrapolated for each time value on the extension of the straight line whose slope is the rate constant of the decarboxylation. In these spectrophotometric determinations, the concentration of carbazate amounted to 5×10^{-5} mol dm^{-3}, which was achieved by introducing 0.03 cm^3 of a stock dioxane solution into a quartz cell containing 3 cm^3 of a sodium hydroxide solution of fixed concentration. Because of the very poor solubility of alkyl phenylcarbazates in sodium hydroxide solutions, we used 25% (v/v) dioxane–water to carry out our kinetic studies.

Working with a water–dioxane medium requires that the pH be calculated from the physicochemical characteristics of this medium, *i.e.* the autoprotolytic constant of water $pK_w = 14.83$ and the activity coefficient $\gamma_{OH^-} = 0.4325$ at 25 °C.[3] pH values exceeding 12 were calculated using eqn. (1).

$$pH = pK_w + \log(\gamma_{OH^-}) + \log[OH^-] \qquad (1)$$

The end-products of the hydrolytic reaction were identified using a macroscopic reaction with 0.4 g of trichloroethyl phenylcarbazate in the presence of 0.2 mol dm^{-3} sodium hydroxide. At the end of the hydrolysis, the medium was acidified with hydrochloric acid and the water–dioxane phase containing the hydrolytic product was evaporated under vacuum. The crystallized product was identified as phenylhydrazine by comparison of the R_f values on TLC. The NMR chemical displacements (solvent DMSO) of the end-products ($\delta_{NHNH_2} = 4.4$; $\delta_{ArH} = 7.0$; $\delta_{NH_3^+} = 10.5$) revealed the presence of a mixture of free phenylhydrazine ($\delta_{NHNH_2} = 4.5$; $\delta_{ArH} = 7.0$) and its hydrochloride ($\delta_{ArH} = 7.0$; $\delta_{NH} = 8.2$; $\delta_{NH_3^+} = 10.5$). The IR spectra showed two narrow and large bands at 3208 and 2699 cm^{-1}, similar to those of phenylhydrazine hydrochloride.

Results

Effect of pH.—In the case of the trichloroethyl phenylcarbazate, the rate constants found at 25 °C for an ionic strength $\mu = 1$ (KCl) are given *vs.* pH. The plot in Fig. 1 showing the dependence of log k_{obs} on pH has two sections, a linear section with a slope equal to 1, followed by a plateau.

Effect of Temperature: Activation Entropy.—The rate constants were determined for the hydrolytic reaction of trichloroethyl *N*-phenylcarbazate at three temperatures in a 0.1 mol dm^{-3} NaOH solution (25 °C, $k_{obs} = 1.62 \times 10^{-3}$ s^{-1}; 35 °C, $k_{obs} = 3.09 \times 10^{-3}$ s^{-1}; 45 °C, $k_{obs} = 5.5 \times 10^{-3}$ s^{-1}). From these results we determined the activation energy, $E_a = 10.07$ kcal mol^{-1}, and the activation entropy, $\Delta S^\ddagger = -39.8$ cal mol^{-1} K^{-1}.

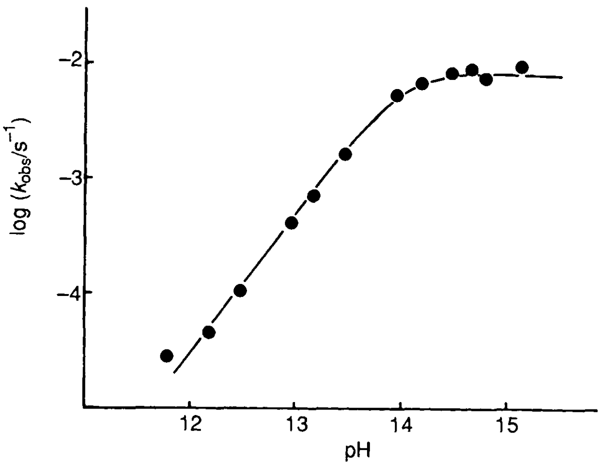


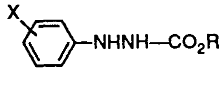
Fig. 1 Dependence of log k_{obs} on pH in the hydrolysis of trichloroethyl *N*-phenylcarbazate at 25 °C at an ionic strength $\mu \geqslant 1$ (KCl)

Table 1 Effect of buffer concentration on the rate of hydrolysis of trichloroethyl *N*-phenylcarbazate at 50 °C for an ionic strength μ = 1 (KCl)

	$r^b = 1$		$r = 2$	
$[B_t]^a$/mol dm^{-3}	pH	$k_{obs}/10^{-4}$ s^{-1}	pH	$k_{obs}/10^{-4}$ s^{-1}
0.14	11.78	3.21	11.88	4.52
0.10	11.79	2.40	11.90	3.53
0.06	11.79	2.01	11.90	3.10
0.02	11.77	1.99	11.87	2.87

[a] $[B_t] = [PO_4^{3-}] + [HPO_4^{2-}]$; [b] $r = [PO_4^{3-}]/[HPO_4^{2-}]$.

Table 2 Rate constants k_{OH^-} (dm^3 mol^{-1} s^{-1}) at 25 °C in the hydrolysis of alkyl *N*-phenylcarbazates



X	R	pK_a (ROH)	$k_{OH^-}/10^{-3}$ dm^3 mol^{-1} s^{-1}
Series I			
H	CH_2CCl_3	12.34	19.2 (r = 0.99; s = 7.8 × 10^{-4})
H	CH_2CH_2Cl	14.31	9.5 (r = 0.99; s = 2.1 × 10^{-4})
H	CH_3	15.54	8.5 (r = 0.99; s = 0.9 × 10^{-4})
H	CH_2CH_3	16.00	6.2 (r = 0.99; s = 0.5 × 10^{-4})
Series II			
4-Cl	CH_2CCl_3	12.24	9.7 (r = 0.98; s = 7 × 10^{-4})
4-Cl	CH_3	15.54	8.0 (r = 0.99; s = 2 × 10^{-4})
4-Cl	CH_2CH_3	16.00	6.8 (r = 0.99; s = 0.7 × 10^{-4})
4-Cl	$CH_2CH_2CH_3$	16.50^a	4.1 (r = 0.99; s = 0.5 × 10^{-4})

[a] S. Takahashi, L. A. Cohen, H. K. Miller and E. G. Peake, *J. Org. Chem.*, 1971, **36**, 1205.

Isotope Effect.—The hydrolytic rate constants for trichloroethyl phenylcarbazate were determined at 25 °C for various NaOH and NaOD concentrations. We found an isotope effect k_{OH^-}/k_{OD^-} = 3.45 for the linear section of slope 1 and an isotope effect k_{H_2O}/k_{D_2O} = 3.69 for the plateau section.

Investigation of General Acid–Base Catalysis.—Considering the high value of the ratio k_{H_2O}/k_{D_2O} describing the isotope effect, we investigated a general catalysis for the hydrolytic reaction using a disodium phosphate buffer for pH values near 12 at 50 °C (Table 1). The hydrolytic rate constants for trichloroethyl *N*-phenylcarbazate were determined for a ratio $[PO_4^{3-}]/[HPO_4^{2-}]$ = 2 and for a ratio $[PO_4^{3-}]/[HPO_4^{2-}]$ = 1 using the relation given in eqn. (2). The catalytic constants

$$v = k'[B_t] + k_o \qquad (2)$$

k' for r = 2 and r = 1 were, respectively, 13.44 × 10^{-4} dm^3 mol^{-1} s^{-1} and 9.09 × 10^{-4} dm^3 mol^{-1} s^{-1}.

When the catalytic constant k' is plotted *vs.* the ratio $[B]/[B_t]$, the value of the catalytic constant of the base $k_{PO_4^{3-}}$ is found to be equal to 1.9 × 10^{-3} dm^3 mol^{-1} s^{-1} and that of the acid $k_{HPO_4^{2-}}$ to 0.

Brønsted Relationship: Effect of the Nature of the Leaving Group.—The study of the rate constant $k_{OH^-} = k_{obs}/[OH^-]$ was conducted in the pH range where the rate is proportional to the OH$^-$ ion concentration. In order to determine the effect of the leaving group, we tried to determine a Brønsted correlation between log k_{OH^-} and the pK_a of the leaving group. Results are given in Table 2.

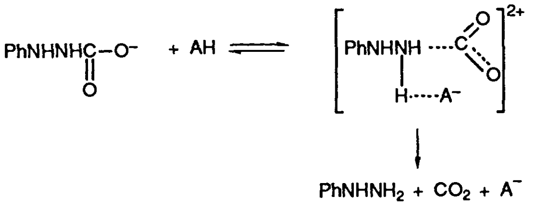
These results revealed two Brønsted correlations [eqns. (3) and (4)].

$$k_{OH} = -0.12\,pK_a - 0.27 \qquad (3)$$
$$(r = 0.98; s = 0.05) \quad \text{for series I}$$

$$k_{OH} = -0.07\,pK_a - 1.10 \qquad (4)$$
$$(r = 0.77; s = 0.13) \quad \text{for series II.}$$

Effect of the Substituent on the Aromatic Ring.—We selected five substituents, with Hammett parameters, σ, ranging from 0–0.75. From the graphs of log $k_{obs}(x)$ *vs.* $f(\sigma)$, we obtain (i) in 0.5 mol dm^{-3} NaOH: log $k_{obs}(x) = -0.89\sigma - 2.20$ (r = 0.93; s = 0.12); (ii) in 10^{-2} mol dm^{-3} NaOH: log $k_{obs}(x) = -0.07\sigma - 4.18$ (r = 0.71; s = 0.03). We determined the Hammett values, ρ, for the two sodium hydroxide concentrations (0.5 and 0.01 mol dm^{-3}). Results are given in Table 3.

Decarboxylation Rate Constants.—In the case of low concentrations of sodium hydroxide, two successive reactions were found to occur; the first one was the formation of the carbazate anion and the second one the decarboxylation of the anion according to the reaction shown in Scheme 1.



Scheme 1

The decarboxylation took place *via* acid catalysis.[4] Some decarboxylation constants were determined in sodium hydroxide ([NaOH] = 2 × 10^{-2} mol dm^{-3}, k_{obs} = 1.56 × 10^{-4} s^{-1}; [NaOH] = 10^{-2} mol dm^{-3}, k_{obs} = 6.15 × 10^{-4} s^{-1}; [NaOH] = 5 × 10^{-3} mol dm^{-3}, k_{obs} = 9.06 × 10^{-4} s^{-1}). These values are of the same order as that obtained for the decarboxylation of carbamic acids[5] ($k_{obs} \approx 10^{-5}$ s^{-1}).

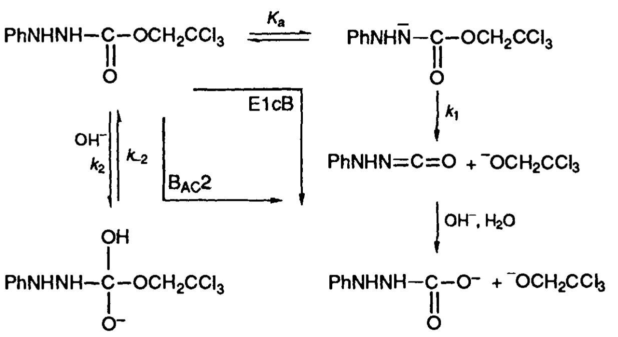
Discussion

As in the case of carbamates, two mechanisms, E1cB and B$_{Ac}$2, can be considered for the hydrolytic reaction of alkyl phenylcarbazates (Scheme 2).

The rates for these two reaction schemes are given by eqn. (5) for the E1cB mechanism and eqn. (6) for the B$_{Ac}$2 mechanism,

Table 3 Rate constants k_{obs} (s^{-1}) at 25 °C for sodium hydroxide concentrations of 0.5 mol dm^{-3} and 0.01 mol dm^{-3} in the hydrolysis of trichloroethyl *N*-phenylcarbazates

	$k_{obs}/10^{-3}$ s^{-1}				
[NaOH]/ mol dm^{-3}	X = H $\sigma = 0$	X = *p*-Cl $\sigma = 0.23$	X = *p*-F $\sigma = 0.34$	X = *p*-CF$_3$ $\sigma = 0.54$	X = 3,5-Cl$_2$ $\sigma = 0.75$
0.50	6.83	4.5	2.08	2.38	1.41
0.01	0.067	0.062	0.062	0.080	0.058



Scheme 2

$$k_{obs} = \frac{k_1 K_a}{K_a + a_H} \quad (5)$$

$$k_{obs} = \frac{k_2 K_w}{K_a + a_H} \quad (6)$$

where a_H is the protonic activity in the medium and K_w the ionic product of water.

The profile of the plot in Fig. 1 is in agreement with the two general equations given above, as shown by the linear section with a slope equal to 1 ($\log k_{obs} = \mathrm{pH} + \log k_1 K_a$) followed by a plateau ($\log k_{obs} = \log k_1$) for the ElcB mechanism. For the B$_{AC}$2 mechanism, the linear section of slope 1 obeys eqn. (7), while that for the plateau section obeys eqn. (8). The pH

$$\log k_{obs} = \mathrm{pH} + \log k_2 K_w \quad (7)$$

$$\log k_{obs} = \log k_2 K_w - \log K_a \quad (8)$$

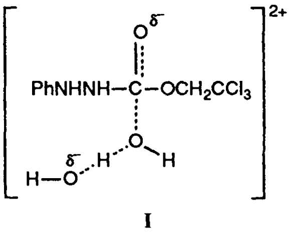
value at the intersection point of the two sections is equal to the pK_a of the compound, *i.e.* 14.12 for trichloroethyl *N*-phenylcarbazate.

These two mechanisms cannot be discriminated kinetically, they differ from each other only by the formation of phenyl isocyanate in the E1cB reaction. Because of its very high reactivity, the presence of this intermediate could not be verified. Therefore, other means were needed for elucidating the reaction mechanism.

The Brønsted relation $\log k_{OH} = f(\mathrm{p}K_a)$ makes it possible to evaluate the influence of the leaving groups on the bimolecular hydrolytic constant of the substrate by means of the pK_a. The Brønsted slope, β, is characteristic of the mechanism involved. For series I and II, the β values are, respectively, -0.12 and -0.07; the absolute values are slightly lower than those found for the hydrolysis of alkyl *N*-acetylcarbamates ($\beta = -0.23$)[6] or of alkyl *N*-methyl-*N*-phenylcarbamates ($\beta = -0.25$).[7] These low values are typical of the B$_{AC}$2 mechanism, while in the case of an E1cB mechanism the β values are close to -1.32.[6]

The relatively high value of the isotope effect in the plateau of Fig. 1 (*i.e.* $k_{H_2O}/k_{D_2O} = 3.69$) rules out the occurrence of the ElcB mechanism. In this pH range $k_{obs} = k_1$ and the unimolecular decomposition of the anion, since it does not include a proton transfer, should exhibit an isotope effect close to 1.

In the hypothesis of a B$_{AC}$2 mechanism, the isotope effect k_{OH^-}/k_{OD^-} should be lower than 1 in the pH range corresponding to the straight section of slope 1 of the pH plot, since OD$^-$ is more nucleophilic than OH$^-$. Considering the opposite effect observed (*i.e.* $k_{OH^-}/k_{OD^-} = 3.45$), it appears that a proton transfer is likely in this reaction for the addition of OH$^-$ from a molecule of water (structure **I**). This hypothesis is confirmed by



I

(i) the strongly negative entropy of activation $\Delta S^{\ddagger} \approx -40$ cal mol^{-1} K^{-1}, which is in agreement with the loss of degrees of freedom for OH$^-$ and for H$_2$O in the transition state; (ii) the general-base catalysis observed with the phosphate buffer. In this reaction, the OH$^-$ ion is replaced by PO$_4{}^{3-}$.

As for the B$_{AC}$2 mechanism in the plateau section of the curve, we have a composite isotope effect [eqn. (9)].

$$\frac{k_{obs}^{H_2O}}{k_{obs}^{D_2O}} = \left(\frac{k_2^{H_2O}}{k_2^{D_2O}}\right)\left(\frac{K_w^{H_2O}}{K_w^{D_2O}}\right)\left(\frac{K_a^{D_2O}}{K_a^{H_2O}}\right)$$

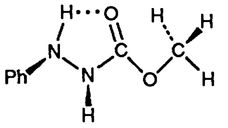
If $$\frac{K_w^{H_2O}}{K_w^{D_2O}} = 7.5 \text{ at } 25\ ^\circ\mathrm{C} \quad (9)$$

and assuming that this effect is approximately counterbalanced by that of $K_a^{D_2O}/K_a^{H_2O}$, the value of $k_{obs}^{H_2O}/k_{obs}^{D_2O} = 3.69$ in the plateau section is primarily due to the ratio $k_2^{H_2O}/k_2^{D_2O} = 3.45$, determined in the straight-line section of slope 1. The value of $K_a^{H_2O}/K_a^{D_2O}$ which is close to 7.0 can be calculated from this relation.

This large value appears reasonable if, according to Bell,[9] the difference $\mathrm{p}K_a^{D_2O} - \mathrm{p}K_a^{H_2O}$ increases as the corresponding pK_a increased.[10] In this case, $\mathrm{p}K_a^{H_2O} = 14.12$ and an isotope effect of the same order as that determined for $K_w^{H_2O}/K_w^{D_2O}$ is not unreasonable. For the acidities of phenols and alcohols, $K_a^{H_2O}/K_a^{D_2O}$ is close to 5 for compounds of pK_a near 14.[11] This value is lower than that we have estimated, the difference being perhaps due to the solvent water–dioxane in which $K_w^{H_2O}/K_w^{D_2O}$ is unknown.

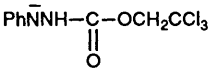
Hammett Values ρ *for the Effect of the Substituent on the Aromatic Ring.*—In 0.01 mol dm^{-3} sodium hydroxide, $\rho = -0.07$. In this low basic medium, $K_a \ll a_H$, so $k_{obs} = k_2K_w/a_H = k^2a_H$: the rate-determining step is the addition of H$_2$O catalysed by OH$^-$. The low ρ value can be explained if the resonance between the phenyl and the carbonyl groups is made unlikely by the configuration of the molecule. So according to a structural study bearing upon the configuration of methyl hydrazine carboxylate,[12] it can be assumed that the most probable configuration is that of structure **II**.

In 0.5 mol dm^{-3} sodium hydroxide, $\rho = -0.89$. In this case, $K_a \gg a_H$, so $k_{obs} = k_2K_w/K_a$ for the B$_{AC}$2 mechanism. Since ρ is low for the addition of water of rate constant k_2, this value



II

reflects the substituent effect for the protonation of the anion **III**. A constant of a similar order of magnitude was found by Stroh and Westphal ($\rho = -1.21$) for the effect of substituent on the protonation of phenylhydrazines.[13]



$\text{Ph}\bar{\text{N}}\text{NH}-\underset{\underset{\text{O}}{\|}}{\text{C}}-\text{OCH}_2\text{CCl}_3$

III

In conclusion, all the evidence presented above points to the fact that the hydrolysis of alkyl *N*-phenylcarbazates takes place in alkaline media according to a $\text{B}_{\text{AC}}2$ mechanism, as in the case of alkyl carbamates. However, features specific to carbazates were found during this study, particularly the high value of the isotope effect and the occurrence of a general-basic catalysis.

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References

1 T. Strumpf and D. Zanke, DDP 243 493/1987.
2 R. Sandmeier and A. Weiss, FRP 2 499 074/1982.
3 F. Coussemant, M. Hellin and B. Torck, *Les Fonctions d'Acidité et leurs Utilisations en Catalyse Acido-Basique*, Gordon and Breach, Paris, 1969, p. 112.
4 M. Al Sabbagh, M. Calmon and J. P. Calmon, *J. Chem. Soc., Perkin Trans. 2*, 1987, 929.
5 S. L. Johnson and D. L. Morisson, *J. Am. Chem. Soc.*, 1972, **94**, 1323.
6 M. Bergon and J. P. Calmon, *Bull. Soc. Chim. Fr.*, 1976, 797.
7 A. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1973, 1244.
8 P. Salomaa, *Acta Chem. Scand.*, 1971, **25**, 367.
9 R. P. Bell, *The Proton in Chemistry*, Cornell University Press, Ithaca, New York, 1959, ch. 11.
10 P. M. Laughton and R. E. Robertson, in *Solute–Solvent Interactions*, eds. J. F. Coetzee and C. D. Ritchie, Dekker, New York, 1969, ch. 7.
11 W. P. Jencks, *Catalysis in Chemistry and Enzymology*, McGraw-Hill, New York, 1969, p. 251.
12 W. Caminati, A. C. Fantoni, L. Schafer, K. Siam and C. Van Alsenoy, *J. Am. Chem. Soc.*, 1986, **108**, 4364.
13 H. H. Stroch and G. Westphal, *Chem. Ber.*, 1963, **96**, 184.

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