Bulletin of the Chemists and Technologists of Macedonia, Vol. **18**, No. 1, pp. 15–20 (1999)
GHTMDD – 321 ISSN 0350 – 0136
Received: December 12, 1998 UDC: 547.584 : 542.949.41.094.7]: 543.422
Accepted: April 14, 1999

Original scientific paper

SPECTROPHOTOMETRIC STUDY OF KINETICS OF ALKALINE HYDROLYSIS OF SOME *N*-SUBSTITUTED PHTHALIMIDES

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The kinetics of the hydrolysis of *N*-(4-R-phenylaminomethyl)-phthalimide (R = H; OCH_3; CH_3; Cl; Br) were studied spectrophotometrically in aqueous sodium hydroxide solutions. The rate of hydrolysis shows a small dependence on the concentration of hydroxide ion in the pH region 9.35–13.70. The effect of para substituent (R) on benzene ring on the reaction rate constants of hydrolysis obeys Hammett`s relationship.

Key words: *N*-substituted phthalimides; alkaline hydrolysis; kinetics

INTRODUCTION

Imides have been of considerable interest for many years because of the medicinal and the biochemical importance of several compounds containing imide functionality. Phthalimide derivatives are used as insecticides [1], fungicides [1, 2], carcinostatics [3–5], anticonvulsants [6].

In alkaline medium occurs the cleavage of imide bond. Khan [7] studied the kinetics of alkaline hydrolysis of *N*-alkylphthalimides with an aim to explore the effect of substituents on this reaction. The mechanisms of aqueous cleavage of succinimide [8] and phthalimide [9] in highly alkaline media have been reported.

The aim of the present work was to determine the reaction rate constants and to investigate the effect of substituents on the benzene ring on alkaline hydrolysis of some *N*-(phenylaminomethyl)-phthalimide derivatives.

EXPERIMENTAL

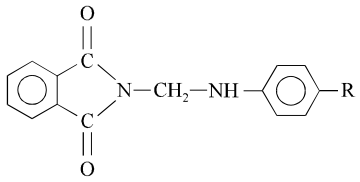
N-(phenylaminomethyl)-phthalimide derivatives (Table 1) were synthesized according to the standard procedure [10] and characterized by melting points, IR and NMR spectra and elemental analysis. Stock solutions of investigated compounds ($2\cdot10^{-3}$ mol·dm^{-3}) were prepared by dissolving the required amounts of the substances in ethanol. All of the chemicals used were of analytical grade purity and all solutions were prepared with demineralised water.

Spectrophotometric measurements were carried out on a Varian Cary 219 spectrophotometer in 1 cm quartz cells. The pH values (7–12) of the solutions were measured on an ISKRA MA-5704 pH-meter. Above this pH range acidity functions for concentrated solutions of NaOH were used [11].

All the kinetic runs were carried out at 25 °C, in a thermostated cell compartment. For a typical kinetic run, the reaction mixture containing all the reaction ingredients except phthalimide was equilibrated at desired temperature. The reaction was then initiated by adding the appropriate amount of phthalimide stock solution so the concentration of the reagent in the reaction mixture was $1.2\cdot10^{-5}$ mol·dm^{-3}. The reference was an alkaline solution (at 25 °C) which contained the same quantity of ethanol as the measured solution. The ionic strength (I = 0.1 mol·dm^{-3}) of all the solutions was kept constant using sodium perchlorate.

Table 1

The structures of compounds studied



1. R = H	*N*-(phenylaminomethyl)-phthalimide
2. R = OCH_3	*N*-(4-methoxyphenylaminomethyl)-phthalimide
3. R = CH_3	*N*-(4-methylphenylaminomethyl)-phthalimide
4. R = Cl	*N*-(4-chlorophenylaminomethyl)-phthalimide
5. R = Br	*N*-(4-bromophenylaminomethyl)-phthalimide

RESULTS AND DISCUSSION

The hydrolysis of investigated phthalimides was studied by following the changes in the electronic absorption spectra recorded in aqueous sodium-hydroxide solutions as a function of time.

The aqueous solutions of investigated compounds show the absorption maxima at about 200, 220 and 290 nm (Fig. 1, Table 2). The last two wavelengths are the typical for the absorption maxima of cyclic imide group of phthalimides [1]. In alkaline media at these wavelengths the intensity of the absorption decrease with the progress of the reaction (Fig. 1). In the absorption spectra clear isosbestic points occur at about 205 nm and about 255 nm, depending on the compound.

A decrease of the intensity of absorption at the absorption maxima which are characteristic of imide ring, with the progress of the reaction, clearly indicates the cleavage of imide bond during the alkaline hydrolysis of *N*-substituted phthalimides.

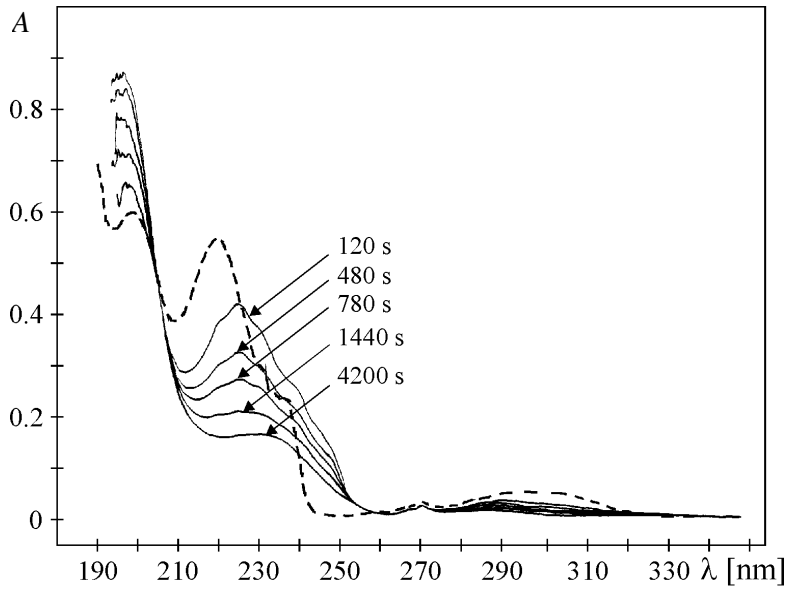


Fig.1. Absorption spectra of *N*-(4-methylphenylaminomethyl)-phthalimide recorded in: - - - - water solution; —— aqueous solution of NaOH (pH = 10.60) as a function of time

Table 2

The spectral characteristics of investigated compounds

Compound	λ_{max} nm	$\varepsilon_{max} \cdot 10^{-3}$ $dm^3\ mol^{-1}\ cm^{-1}$
1	197; 219.5; 237.5; 289	44.2; 44.6; 15.8; 2.95
2	193; 219; 237.5; 296	49.2; 46.0; 17.5; 4.18
3	199; 219; 237.5; 291	51.8; 47.6; 18.4; 3.34
4	199; 219; 238; 295	45.0; 41.2; 18.4; 3.61
5	200; 219; 238; 296	45.6; 42.8; 19.8; 3.49

The kinetics of alkaline hydrolysis of *N*-(phenylaminomethyl)-phthalimide derivatives were studied within the pH-range of 9.35 to 13.70 (Fig. 2).

The reaction rates were found to obey a simple pseudo-first-order rate law and the observed pseudo-first-order rate constants, k_{obs}, were calculated from equation (1).

$$k_{obs} = \frac{1}{t} \ln \frac{A_o - A_\infty}{A - A_\infty} . \qquad (1)$$

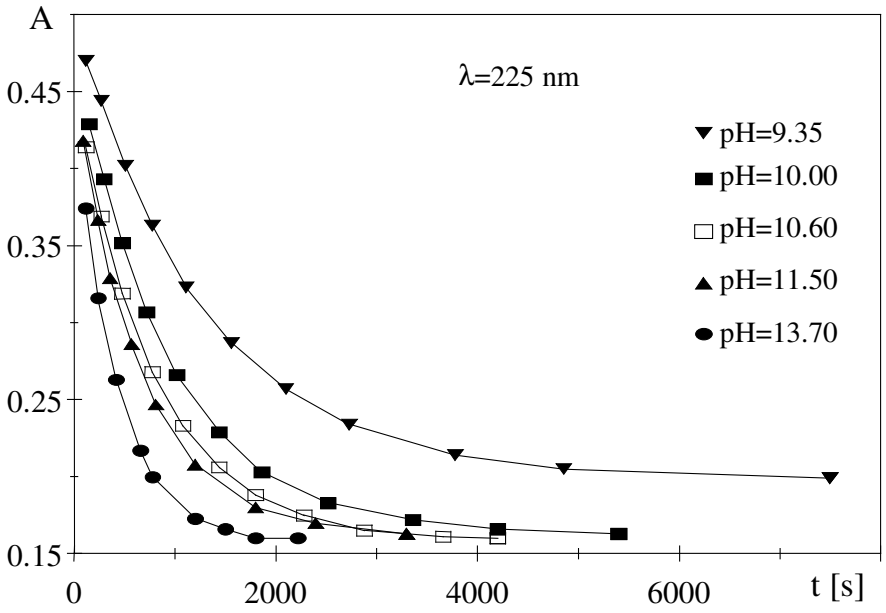


Fig. 2. The absorbance changes of the solutions of substance 1 on the time at the different pH values of the solutions

A_o is the absorbance of solution before the beginning of the reaction, A_∞ is the absorbance of solution after the end of the reaction, and A is the absorbance of the solution at time t, at the same wavelength λ. A_o and A_∞ were determined by extrapolation using the interpolation polynoms constructed from the kinetic data.

The calculated rate constants are presented in Table 3. The rate constants of the alkaline hydrolysis of investigated compounds show a small dependence on the pH values of the solutions. The values of k_{obs} slightly increase with the progress of basicity of the medium.

For a series of *N*-alkylmaleimides Matsui *et al.* [11] calculated the hydroxide ion-catalysed rate constants, k_{OH^-}, in the pH region 7.02–9.26, from equation (2):

$$\log k_{obs} = \log\left(k_{OH^-} \cdot K_w\right) + \text{pH} . \qquad (2)$$

Our unpublished results show a linear relationship between $\log k_{obs}$ of alkaline hydrolysis of *N*-(phenylaminomethyl)-phthalimide and pH in the pH range 8.52 – 9.80, with the slope equals unity.

Table 3

The values of the reaction rate constants, $k_{obs}\cdot10^3$ s^{-1}, for the studied compounds

pH	Compound				
	1	**2**	**3**	**4**	**5**
9.35	0.809 ± 0.007	0.756 ± 0.008	0.775 ± 0.006	0.856 ± 0.005	0.862 ± 0.005
10.00	1.080 ± 0.020	1.026 ± 0.025	1.040 ± 0.020	1.121 ± 0.028	1.135 ± 0.015
10.60	1.309 ± 0.016	1.260 ± 0.018	1.281 ± 0.009	1.350 ± 0.025	1.355 ± 0.018
11.50	1.596 ± 0.020	1.483 ± 0.017	1.529 ± 0.025	1.691 ± 0.011	1.701 ± 0.017
13.70	2.528 ± 0.010	2.389 ± 0.017	2.449 ± 0.029	2.650 ± 0.024	2.661 ± 0.023

The observed reaction rate constants of *N*-(4-R-phenylaminomethyl)-phthalimides at the different pH values (9.35 – 13.70) do not fit the equation (2). In this region reaction rate slowly changes with increasing pH value and dependencies of $\log k_{obs}$ on the pH in region pH 10.00 – 13.70 fit the empirical equation (3):

$$\log k_{obs} = a + b \cdot \mathrm{pH} \qquad (3)$$

where for all of investigated compounds *a* and *b* have values of about –3.9 and 0.1, correspondingly. This fact is a proof that the rates of alkaline hydrolysis of investigated phthalimides up pH 10 are almost independent on the concentration of hydroxide, which is in agreement with literature data for hydrolysis of other imides in solution of high pH values [13].

The effect of para substituents on benzene ring on alkaline hydrolysis of substituted phthalimides could be seen from the plots of $\log k_{obs}$ versus Hammett`s substituent constants σ. The plots are linear (Fig. 3) with the slopes, ρ, of about 0.1 (Table 4). The electron-attracting substituents (p-Cl and p-Br) accelerate and the electron-donating groups (p-OCH_3 and p-CH_3) slow down the hydrolysis, having reference to unsubstituted compound.

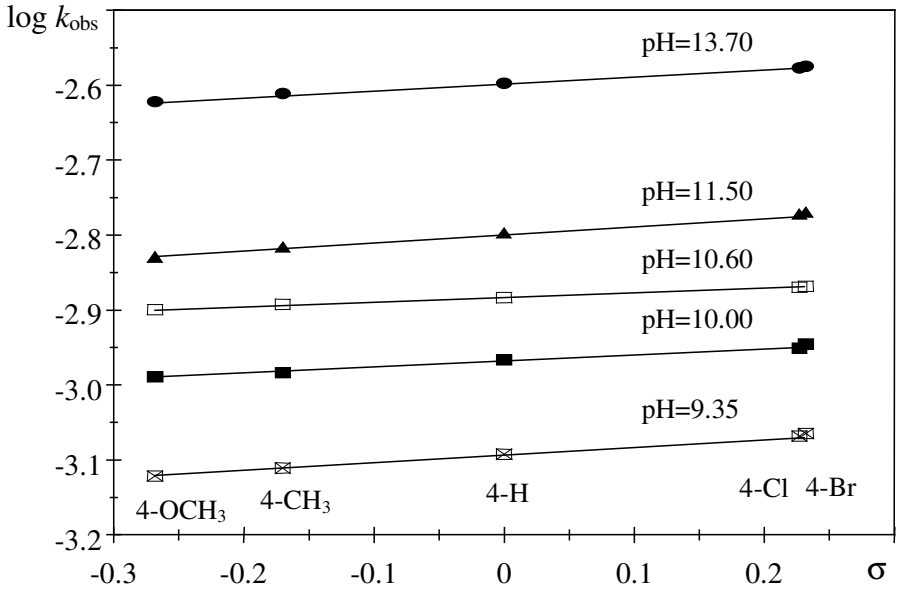


Fig. 3. Plots of $\log k_{obs}$ versus Hammett`s substituent constants σ for alkaline hydrolysis of *N*-(phenylaminomethyl)-phthalimide derivatives

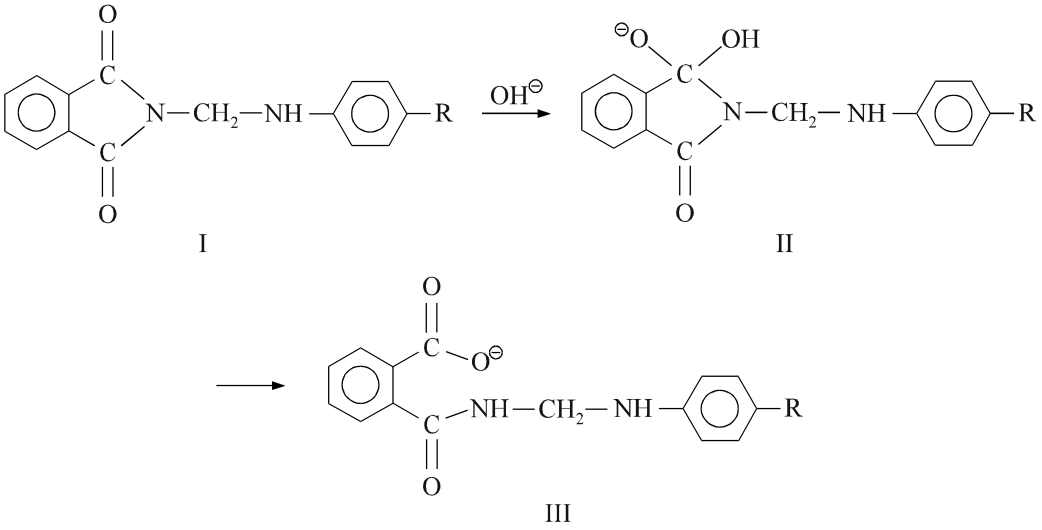
Table 4

The values of the reaction constants ρ at the different pH values

pH	9.35	10.00	10.60	11.50	13.70
ρ	0.112	0.085	0.061	0.116	0.091
	± 0.002	± 0.005	± 0.002	± 0.003	± 0.002

It is well known that $\rho > 0$ for all of the reactions facilitated by the presence of electron-attracting substituents. Positive values of reaction constants ρ, indicate that the nucleophilic attack is the rate-determining step in the alkaline hydrolysis of *N*-aryl substituted phthalimides. The low values of ρ show that substituents which are far from the reaction centre have a small influence on the reaction rate.

On the basis of the literature data [12,14] and our results, we proposed the reaction mechanism presented in the Scheme 1.



Scheme 1

Formation of intermediate II by nucleophilic attack of hydroxide ion on the carbonyl carbon of the imide ring is the rate-determining step

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Р е з и м е

СПЕКТРОФОТОМЕТРИСКО ПРОУЧУВАЊЕ НА КИНЕТИКИТЕ НА АЛКАЛНА ХИДРОЛИЗА НА НЕКОИ *N*-СУПСТИТУИРАНИ ФТАЛИМИДИ

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Клучни зборови: *N*-супституирани фталимиди; алкална хидролиза; кинетика

Спектрофотометриски беа изучувани кинетиките на хидролиза на *N*-(4-R-фениламинометил)-фталимид (R=H; OCH_3; CH_3; Cl; Br) во водни раствори на натриум хидроксид. Степенот на хидролизата покажува мала зависност од концентрацијата на хидроксидниот јон во pH со опсег 9,35 – 13,70. Ефектот на супституентите во бензенското јадро врз реакциониот степен на константите на хидролиза е во корелација со Hammett-овата равенка.