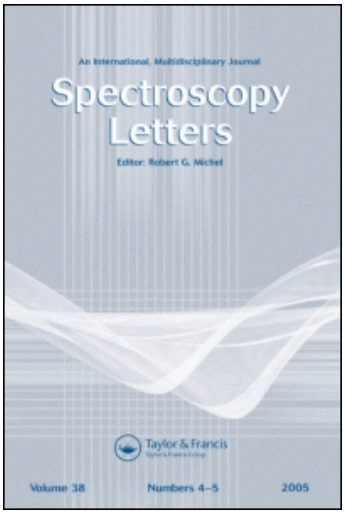

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Spectrophotometric Study of the Protonation Processes of Some: N-(4-X-Phenylaminomethyl)-phthalimide Derivatives

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SPECTROPHOTOMETRIC STUDY OF THE PROTONATION PROCESSES OF SOME N-(4-X-PHENYLAMINOMETHYL)-PHTHALIMIDE DERIVATIVES

Key words: N-(4-X-phenylaminomethyl)-phthalimide derivatives, UV spectrophotometry, protonation constants

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ABSTRACT

The protonation of N-(4-X-phenylaminomethyl)-phthalimide derivatives and phthalimide in aqueous acidic (H_2SO_4) media was investigated, using the spectrophotometric method. These phthalimide derivatives have three protonation processes. The first protonation process occurs in pH range and belongs to the protonation of amino-group. The second and the third protonation process (occur in concentrated sulfuric acid solutions) are overlapping processes. They were separated by the modified method of separation (Garcia et al.). The protonation constants were calculated by Hammett and Cox-Yates method. The effect of chemical structure on ionisation constants is discussed.

INTRODUCTION

Phthalimides represent a group of organic compounds with a large biological activity. Some of these compounds are used as fungicides[1,2], insecticides[1], carcinostatics[3-5], anticonvulsants[6].

In acidic media phthalimide and its derivatives act as very weak bases[7], but there are no data in literature about the protonation constants of phthalimides.

Thus the aim of this paper was to investigate the protonation processes of phthalimide and N-(4-X-phenylaminomethyl)-phthalimide derivatives, to determine the protonation constants and to find which of the methods and the acidity functions best describe the protolytic equilibria in strong acidic media.

EXPERIMENTAL SECTION

Materials

The structures of the investigated compounds are presented in *TABLE I.*

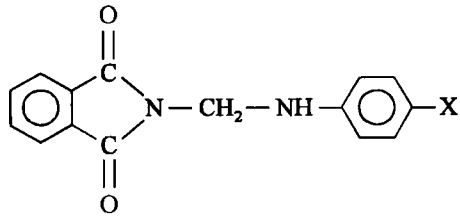
Phthalimide derivatives were prepared as reported[8]. They were characterized by determining melting points and recording IR and NMR spectra, as well as by elemental analysis. Stock substrate solutions (concentration of $2 \cdot 10^{-3}$ mol·dm^{-3}) were prepared in ethanol. The concentration of test aqueous solutions of the investigated compounds during the determination of pK_{BH^+} values was in the range $5 \cdot 10^{-5}$ mol·dm^{-3} to $9 \cdot 10^{-5}$ mol·dm^{-3}, depending on the compound. All other used chemicals were of analitical purity.

Spectral and pH Measurements

Absorption spectra were taken on a VARIAN CARY 219 spectrophotometer in 1 cm quartz cells, at 25°C. The spectra were recorded in acidity range from pH 7 to 92% H_2SO_4. The reference was an acid solution which contained the same quantity of ethanol as the measured solution.

In pH range the ionic strength was kept constant by the addition of sodium perchlorate (I = 0.1 mol·dm^{-3}). The pH values of solutions in the range of 2-7 were measured by an ISKRA MA-5704 pH-meter. Above this pH range the concentrated sulfuric acid solutions were used. The concentration of solutions were determined from the density measurements at 25°C by precise density meter[9]. H_A[10] and X[11] acidity functions were used for characterization of these solutions.

TABLE 1.
The structures of compounds studied



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

Some authors described, that the protonation of imides in acidic media is accompanied by the ring cleavage[12]. In order to investigate the stability of imides studied, we have prepared the solutions of each imide in concentrated sulfuric acid solution. These solutions were diluted to obtain the defined acid concentration and the spectra were recorded. The same spectra were obtained, as well as by the preparation of the imide solutions in dilute sulfuric acid of the same concentration. The protonation process is reversible, so that the dissociation process of the protonated form and its transformation into the neutral form, can be also followed spectrophotometrically. It shows that there are no ring cleavage or hydrolysis of investigated compounds in strong acidic media at 25°C.

RESULTS AND DISCUSSION

Absorption Spectra

The protonation of phthalimide and N-(4-X-phenylaminomethyl)--phthalimide derivatives was investigated by spectrophotometric method, following

the changes in the electronic absorption spectra of aqueous solutions of phthalimides in sulfuric acid.

The electronic absorption spectra of aqueous solutions of phthalimides are characterized by the presence of three characteristic bands: at 219 nm, 238 nm and between 290 and 300 nm (*FIG. 1, TABLE 2.*). These characteristic band positions are in agreement with the literature data for similar groups of compounds[1,13].

The increase of solution acidity of N-(4-X-phenylaminomethyl)--phthalimide up to 1 mol·dm^{-3} is accompanied by a decrease in the intensity of the absorption maxima of neutral form and a simultaneous batochromic shift of the absorption maxima. These spectral changes belong to the amino group protonation. The increase of acidity from pH 0 to 17 mol·dm^{-3} H_2SO_4 shifts the absorption maximum to longer wavelengths, with increasing of the absorption intensity (*FIG. 2.*).

In the absorption spectra of compound **6** there are no changes in pH range.

The spectral changes of investigated phthalimides are followed by the appearance of the isosbestic points at about 285 nm and about 315 nm.

The plots of absorbancies against pH and acidity functions give sigmoid curves (*FIG. 3.*) and confirmed the formation of three ionic forms.

Characteristic spectral changes in pH range (compounds **1-5**) belong to the amino-group protonation. Spectral changes in more acidic media belong to the protonation of imide part of the molecule.

Calculation of the Protonation Constants

The values of the protonation constants (pK_{BH^+}) of monoprotonated phthalimides **1-5** were calculated from the dependencies of the absorbance vs. pH curves, at several wavelengths, according to the known spectrophotometric method[14]:

$$pK_{BH^+} = \log I + m \cdot pH \qquad (1) \qquad \left(I = \frac{[BH^+]}{[B]} = \frac{A - A_B}{A_{BH^+} - A} \right)$$

on condition that $m = 1$. A_B is the absorbance of unprotonated form, A_{BH^+} is the absorbance of protonated form and A is the absorbance of the solution at the given acidity on the same wavelength λ.

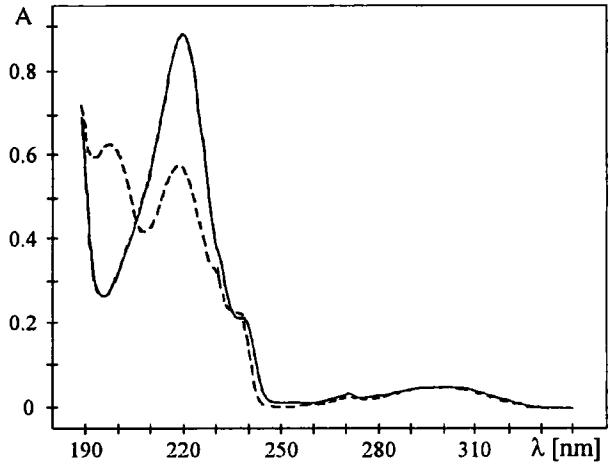


FIG. 1. Absorption spectra recorded in aqueous solutions
—— *phthalimide*
- - - - *N-(4-methylphenylaminomethyl)-phthalimide*

TABLE 2.
The spectral characteristics of investigated compounds

Substance	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
6	219; 238; 298	41.5; 10.5; 2.48

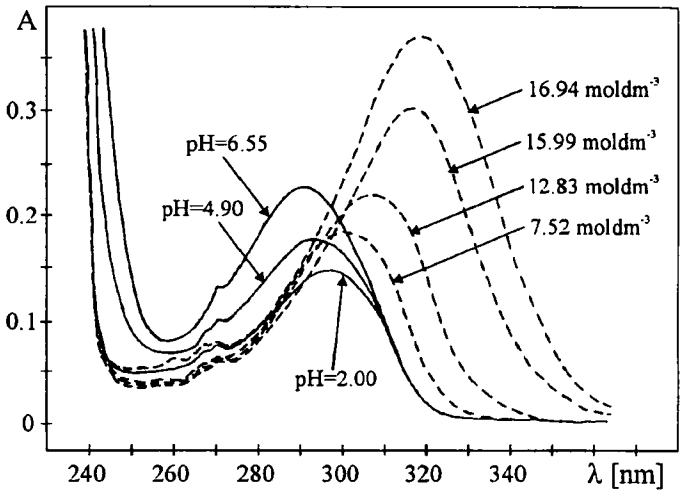


FIG. 2. Absorption spectra of N-(4-methylphenylaminomethyl)-phthalimide as a function of H_2SO_4 concentration

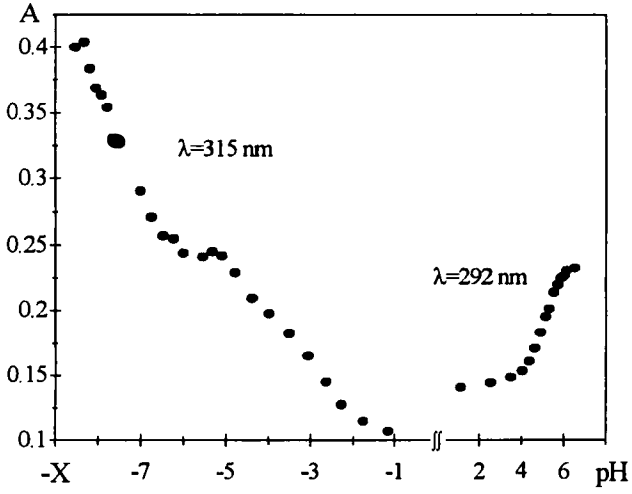


FIG. 3. Absorbance changes of N-(4-methylphenylaminomethyl)-phthalimide as a function of acidity of solutions

The protolytic equilibria in pH range are separated by more than three pK_{BH^+} units from the equilibria in more concentrated acid solutions. The first protonation constants were determined independently, as for monoprotic bases. The results are presented in *TABLE 3.* The protonation on the amino-group, is affected by X-group. The pK_{BH^+} values decrease with the increasing of electron-withdrawing features of substituents.

pK Values in Concentrated H_2SO_4 Solutions

The second and the third protonation process occur in high concentration sulfuric acid solutions and the ionisation constants ($pK_{BH_2^{2+}}$ and $pK_{BH_3^{3+}}$) were determined using two methods:

1. Hammett acidity function method[14] (HAFM)

$$pK_{BH_n^{n+}} = \log I + m \cdot H_X \tag{2}$$

where as H_X was used H_A acidity function[10]

2. "Excess acidity" function method[11] (EAFM)

$$pK_{BH_n^{n+}} = \left(\log I - \log c_{H^+}\right) - m^* \cdot X \tag{3}$$

where X-function is the difference between the observed acidity and that the system would have if it were ideal.

The second and the third protonation process are overlapping processes. These processes were separated using the modified method of separation (Garcia et al.[15]). The original Garcia et al.[15] method is useful for the overlapping equilibria in pH range. In our case the protonation equilibria occur in sulfuric acid solutions of high concentrations. Thus it was necessary to express the concentration of the H^+ ions in the solutions. It was made according to the equation (4):

$$c_{H^+} = 10^X \tag{4}$$

where X is acidity function defined in "excess acidity" function method[11].

In order to separate the overlapping processes the original spectral data were corrected according to the equations (5) and (6):

$$A_{c_1} = \frac{A - \left(C_3 \cdot A_3\right)}{C_1 + C_2} \tag{5}$$

$$A_{c_2} = \frac{A - \left(C_1 \cdot A_1\right)}{C_2 + C_3} \tag{6}$$

TABLE 3.

a) *The values of ionisation constants calculated from the original spectral data*

Sub-stance	pK_{BH^+}	m	HAFM		EAFM		HAFM		EAFM	
			$pK_{BH_2^{2+}}$	m	$pK_{BH_2^{2+}}$	m^*	$pK_{BH_3^{3+}}$	m	$pK_{BH_3^{3+}}$	m^*
1	4.529 ± 0.006	1.007	-2.62 ± 0.04	1.00	-2.68 ± 0.03	0.55	-4.90 ± 0.12	1.03	-6.46 ± 0.03	0.76
2	5.216 ± 0.008	0.994	-2.46 ± 0.04	0.99	-2.51 ± 0.04	0.55	-4.68 ± 0.09	0.76	-5.94 ± 0.04	0.73
3	5.009 ± 0.006	1.008	-2.56 ± 0.02	1.05	-2.62 ± 0.01	0.55	-4.99 ± 0.04	1.00	-6.34 ± 0.02	0.74
4	4.089 ± 0.013	0.993	-2.91 ± 0.01	1.06	-2.84 ± 0.01	0.51	-	-	-	-
5	4.044 ± 0.010	0.998	-2.85 ± 0.04	1.02	-2.84 ± 0.03	0.52	-	-	-	-

b) *The values of ionisation constants calculated from the corrected spectral data*

1	-	-	-2.83 ± 0.07	0.99	-2.65 ± 0.03	0.48	-4.33 ± 0.12	0.85	-4.88 ± 0.09	0.62
2	-	-	-2.77 ± 0.05	0.94	-2.53 ± 0.04	0.46	-4.72 ± 0.12	0.73	-4.69 ± 0.02	0.53
3	-	-	-2.77 ± 0.05	1.05	-2.60 ± 0.05	0.48	-4.95 ± 0.18	0.68	-4.79 ± 0.06	0.52
6	-	-	-2.81 ± 0.08	0.89	-2.53 ± 0.03	0.44	-4.61 ± 0.14	0.74	-4.59 ± 0.04	0.54

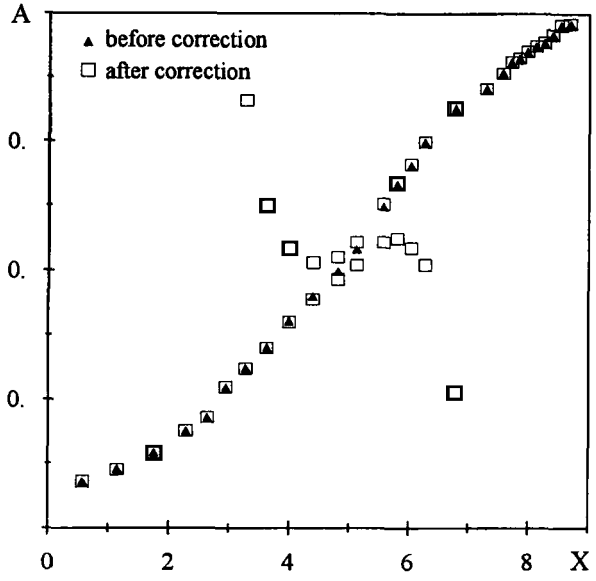


FIG. 4. Absorbance changes of phthalimide as a function of acidity of solutions

where $$C_1 = \left(1 + c_{H^+}^{n_2} \cdot K_2^{-n_2} + c_{H^+}^{(n_1+n_2)} \cdot K_1^{-n_1} \cdot K_2^{-n_2}\right);$$

$$C_2 = C_1 \cdot c_{H^+}^{n_2} \cdot K_2^{-n_2}; \qquad C_3 = 1 - \left(C_1 + C_2\right).$$

A_1 is the absorbance of unprotonated form of molecule, A_3 is the absorbance of diprotonated form, and A is the absorbance of solution of defined acidity, at the same wavelength λ. K_1 and K_2 are the ionisation constants, determined on the basis of uncorrected absorbance values. The uncorrected and the corrected absorbance changes of phthalimide vs. X function are presented in *FIG. 4*.

This method was applied to correct the original spectral data of all investigated compounds except **4** and **5** where the third protonation processes were not completed.

The values of $pK_{BH_2^{2+}}$ and $pK_{BH_3^{3+}}$, calculated from the original and the corrected spectrophotometric data using two methods (equations (2) and (3)), are summarized in *TABLE 3*.

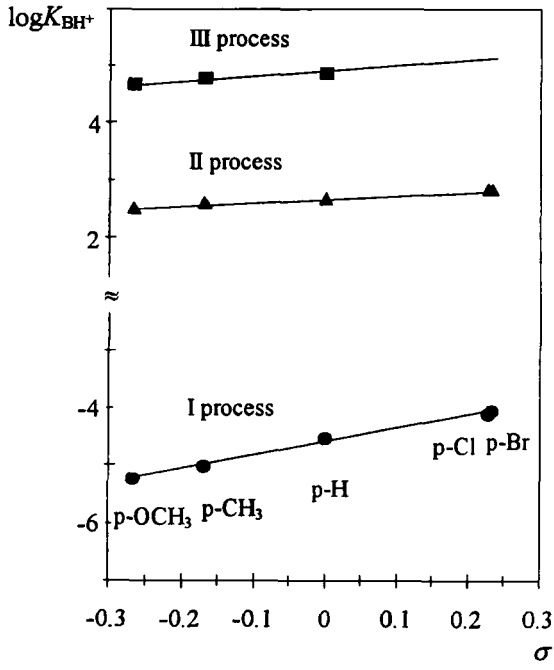


FIG. 5. Plot of $-pK_{BH^+}$ against Hammett's σ values

For the second protonation process the plots of *log I* vs. H_A are linear. The values of the slopes *m* show that the second protonation process (the first protonation process of the imide-group) follows the H_A acidity function. The third protonation process (the second protonation process of imide-system) is not in good agreement with any acidity function of Hammett's type. The results obtained using the EAFM are very close to the values for protonation of oxygen, reported earlier[11].

Substituent Effect

The values of ionisation constants decrease with the increasing of electron-withdrawing features of substituents on the nitrogen atom in phthalimide molecule.

TABLE 4.
The values of the reaction constants ρ

	I Process	II Process		III Process
		I Method	II Method	II Method
ρ	2.33 ± 0.09	0.83 ± 0.10	0.63 ± 0.05	0.69 ± 0.13
r	0.996	0.958	0.982	0.966

(r is the correlation coefficient)

The plots of ionisation constants values of N-(4-X-phenylamino-methyl)-phthalimide derivatives against Hammett`s σ[16] constants are linear (*FIG. 5*) and they are in good agreement with the Hammett[17] equation (7):

$$\log K_{BH^+} = \rho \cdot \sigma + \log K^0_{BH^+} \quad (7)$$

where K_{BH^+} is the ionisation constant of substituted compound and $K^0_{BH^+}$ is the ionisation constant of unsubstituted compound.

The parameters of Hammett equation are listed in *TABLE 4.*

The large value of reaction constant ρ for the first protonation process shows the large substituent effect on the protonation of the amino-group. Much lower values of ρ for the second and the third protonation process are expected because of the distance of substituents from the reaction centre.

From the calculated value of the reaction constant of the third protonation process and on the basis of Hammett`s equation (7), the ionisation constants of compounds **4** and **5** were determined. The obtained pK_{BH^+} values are -5.04 ± 0.03 for compound **4** and -5.05 ± 0.03 for compound **5**.

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