



# Spectrophotometric Determination of the Acidity Dissociation Constants of Symmetric Schiff Base Derivatives

Gülşen TÜRKOĞLU<sup>1</sup>, Halil BERBER<sup>1, \*</sup>, Müjgan YAMAN ÖZKÜTÜK<sup>2</sup>

<sup>1</sup>Chemistry Department, Anadolu University, 26470 Eskişehir, Turkey

<sup>2</sup>Chemistry Department, Eskişehir Osmangazi University, 26040 Eskişehir, Turkey

Received: 04.04.2013 Revised: 07.03.2014 Accepted: 08.04.2014

## ABSTRACT

In this study, the acidity constants of series symmetric Schiff base derivatives have been determined using the UV-visible spectrophotometric method at a temperature of 25(±0.1) °C. The deprotonated acidity constants (pKa) have been found to be associated with the deprotonation of phenolate oxygen. The first and the second protonated acidity constants (pKa1 and pKa2) have been found to cause the protonation of the imine nitrogen atom for all molecules. The deprotonated acidity constants ( $pK_a$ ) were found for molecules **5** (9.088), **8** (9.848), **6** (10.243), **2** (10.2569), **3** (10.297), **1** (10.587), **7** (10.692) and **4** (10.804). The first protonation ( $pK_{a1}$ ) was found for molecules **2** (3.432), **5** (4.207), **8** (4.612), **7** (4.758), **4** (4.995), **1** (5.288), **6** (5.606) and **3** (6.452). The second protonation ( $pK_{a2}$ ) was found for molecules **2** (-5.384), **8** (-5.165), **5** (-5.028), **7** (-4.775), **4** (-4.518), **1** (-4.111), **6** (-3.866) and **3** (-3.212).

**Key Words:** Spectrophotometric determination, Symmetric Schiff base, Acidity Dissociation Constants, UV-spectroscopy

## 1. INTRODUCTION

Schiff bases have been used extensively as ligands in the field of coordination chemistry [1]. These complexes play an important role in the development of coordination chemistry related to catalysis and enzymatic reactions, magnetism and molecular architectures [2]. An important area is the use of Schiff bases in photochromism and thermochromism, which has its roots in the proton

transfer from the hydroxyl *O* atom to the imine *N* atom in the solid state [3-5]. Possessing this particular biological activity gives them an important place in the diverse fields of chemistry and biochemistry [6-9]. Alternatively, the reactive azomethine linkage of a wide range of Schiff bases display inhibitory activity against experimental tumor cells [10,11]. A growing interest in *ortho* hydroxy

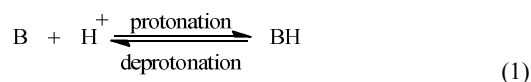
Schiff bases has been observed lately due to their ability to form intramolecular hydrogen bonds by  $\pi$ -electron coupling between their acid-base centers [12-15]. The intermolecular proton transfer reaction proceeds comparatively easily in these compounds. The intermolecular  $\pi$ -electron coupling leads to a strengthening of the hydrogen bonding in these systems [16]. The acidity constants of organic reagents are important in many analytical procedures and research areas such as acid base titration, solvent extraction, ion transport and complex formation [17]. Thus, their accurate determination is often needed for various chemical and biochemical areas [18]. In particular, knowing the accurate acidity constant values provides a key to understanding chemical reactions between the compound of interest and its pharmacological target [18]. This saves time in designing and synthesizing new

candidates which meet the requirements of their intended application.<sup>[18]</sup> Additionally, the  $pK_a$  value(s) of a compound influences many characteristics such as its reactivity, spectral properties (such as its color) and determination of the activity centers of enzymes in its biochemistry [19]. Following our work on the synthesis of certain novel symmetrical Schiff bases [20, 21], we are now able to report on their acid dissociation constants to elucidate structure-reactivity relationships of these novel compounds.

## 2. EXPERIMENTAL

### 2.1. General

Spectrometry is an ideal method [22] when a substance is not soluble enough for the potentiometer or when its  $pK_a$  value is particularly low or particularly high (for example less than 2 or more than 11). The method depends on the direct determination of the ratio of the molecular species, that is, the neutral molecules to the corresponding ionized species in a series of non-absorbing buffer solutions where  $pH$  values are either known or measured. To provide a series of solutions in highly acid and highly basic regions, the acidity functions  $H_0$  and  $H_-$  were used [23]. In strong acid solutions in which the ionic strength is high, the proton-donating ability of the medium is no longer measured by the concentration of hydrogen ions, since the molar activity coefficients of the ions in the solution are not united. As a measure of the acidity degree to which a weak organic base is protonated, Hammett and Deyrup established the  $H_0$  acidity scale [23]. This scale was improved by Jorgensen and Harterr [24] and then Johnson, Katritzky and Shapiro [25]. For weak bases **B** (or weak acids **BH**) ionization process [22,27-29] is



(mono protonation and mono deprotonation), (where charge is neglected)

and the ionization constant,  $K_a$ , is given by

$$K_a = \frac{\alpha_{BH}}{\alpha_B \alpha_{H^+}} \quad (2)$$

the equilibrium constants might be expressed in terms of activity in Eq. (2).

$$\alpha = c \cdot \gamma \quad (\alpha = \text{activity}; \quad c = \text{concentration}; \quad \gamma = \text{activity coefficient}) \quad (3)$$

By inserting the equivalence of Eq. (3) in Eq. (2), we can reach Eq. (4).

$$K_a = \frac{[BH] \gamma_{BH^+}}{[B][H^+] \gamma_B \gamma_{H^+}} = \frac{[BH] \gamma_{BH^+}}{[B] \gamma_B} \alpha_{H^+} \quad (4)$$

By rearranging Eq. (4), we can obtain Eq. (5) (for acidity constants,  $H_x$ ).

$$K_a = \frac{[BH]}{[B]} \cdot h_x \quad (5)$$

$$\text{Bearing in mind that } h_x = \frac{\gamma_{BH^+}}{\gamma_B} \alpha_{H^+}$$

By rearranging Eq. (5), we can obtain Eq. (6).

$$h_x = \frac{K_a [B]}{[BH]} \quad (6)$$

$$H_x = -\log h_x \quad (7)$$

(Where  $H_x$  is an acidity function)

By inserting the equivalence of Eq. (7) in Eq. (6), we can reach Eq. (8).

$$H_x = -\log h_x = -\log \frac{K_a [B]}{[BH]} = -\log K_a - \log \frac{[B]}{[BH]} \quad (8)$$

$$(pK_a = -\log K_a)$$

By rearranging Eq. (8), we can obtain Eq. (9)

$$H_x = pK_a - \log \frac{[B]}{[BH]} \quad (9)$$

$$\text{Bearing in mind that } I = \frac{[B]}{[BH]}$$

By rearranging Eq. (4), we can obtain Eq. (10) (for pH).

$$pH = pK_a - \log \frac{[B]}{[BH]} \quad \text{and} \quad pK_a = pH + \log \frac{[B]}{[BH]}$$

The  $H_0$  scale is defined so that, for the uncharged primary aniline indicators used, the plot of  $\log I$  (i.e.  $\log ([BH]/[B])$ ) against  $H_0$  has unit slope. In our study, we have observed on bases other than the Hammett type that the slopes of the plots of  $\log I$  against  $H_0$ , denoted by  $m$ , were not always united. Thus, a series of structurally similar bases, like triarylmethanols [30], primary amides [31,32] and tertiary aromatic amines [33] defined individual acidity functions,  $H_R$ ,  $H_A$ , and  $H_0''$ , which have a linear relationship to  $H_0$  with  $m$  values of 2.0, 0.6, and 1.3, respectively. Yates proposed that any acidity function  $H_x$  would be proportional to  $H_0$  over the entire acidity range, that is  $H_x = m \cdot H_0$ , with a common point  $H_0 = 0$  [34]. An experimental plot of  $\log I$  against  $H_0$  does not yield the  $pK_a$  at  $\log I = 0$ , unless it is a Hammett base but rather the  $H_0$  at half protonation ( $H_0^{1/2}$ ).

By rearranging Eq. (9), we can obtain Eq. (12).

$$H_x = pK_a - \log I \quad (11)$$

$$pK_a = H_x + \log I \quad (12)$$

$$(\text{if } \log I = 0 \text{ then } H_x = H_0^{1/2})$$

$$pK_a = H_0^{1/2} \quad (13)$$

Mathematically it can be expressed as a straight line ( $y = mx + n$ ) with a slope of  $m$  so it becomes as follows;

$$pK_a = m \cdot H_0^{1/2} \quad (14)$$

Generally, those bases for which  $m$  lies roughly between 0.85 and 1.15 are called ‘‘Hammett Bases’’ and  $m$  is taken as unity. Therefore, it is important to measure  $m$  as well as  $H_0^{1/2}$  for each base studied. It is evident that other acidity functions could exist at the extreme alkaline edge of the pH range, namely, the above pH 14, for measuring the  $pK_a$  values of weak acids and strong bases, the former with an  $H_-$  scale and the latter with an  $H_0$  scale. This is a more difficult region of  $pH$  than the acidic strength dealt with in the foregoing, due to the fact that as the glass electrode becomes increasingly inaccurate and strong,  $OH^-$  absorption swamps the reading. It is well established that the basic properties of aqueous alkalis increase in a nonlinear fashion, with concentration [35]. The use of  $H_-$  in a highly alkaline solution has been described in the literature [36, 37]. The sigmoid curve approach should be carried out carefully in this region to make sure that the function used is a relevant one. Any discussion about the acid dissociation constants in this region should be done by taking into account the half protonation values rather than the  $pK_a$  values.

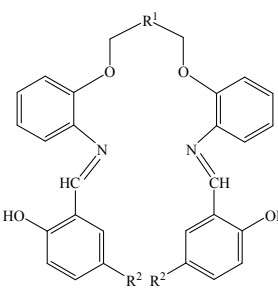
## 2.2. Apparatus and materials

The studied compounds were synthesized in Table 1 and the procedures of the synthesis are described elsewhere [20].

Ethanol, KOH,  $H_2SO_4$ , HCl,  $CH_3COOH$ ,  $CH_3COONa$ , NaOH,  $KH_2PO_4$ ,  $Na_2CO_3$ ,  $NaHCO_3$ , phenolphthalein indicator and standard buffer solutions were not purified further from Aldrich, Fluka and Merck. The  $pH$  measurements were performed using a combined glass electrode. A standard buffer solution of  $pH$  values of 4.01, 7.00 and 10.01 was used in the calibration of the Mettler Toledo Seven Multi Ion  $pH/mV/ORP$  and the Ohaus Adventurer balance. A Perkin Elmer Lambda 35 UV-Vis scanning spectrometer was used for taking measurements.

All of the solutions were prepared fresh on a daily basis. The  $H_2SO_4$  solutions, the KOH solutions and  $pH$  buffer solutions were prepared in water by using methods described in the literature [22,27-29]. The potentiometric measurements were performed by measuring the hydrogen ion concentration (under nitrogen atmosphere) at a temperature of  $25(\pm 0.1)^\circ C$ , and the ionic strengths of the media were maintained at 0.1 using NaCl.

Table 1. Formulas and IUPAC names for the studied compounds 1-8

	No	IUPAC Name	Substituent	
			R <sup>1</sup>	R <sup>2</sup>
	1	2,2'-(((propane-1,3-diylbis(oxy))bis(2,1phenylene))bis(azanylylidene))bis(methanylylidene)diphenol	-CH <sub>2</sub> -	-H
	2	2,2'-(((propane-1,3-diylbis(oxy))bis(2,1-phenylene))bis(azanylylidene))bis(methanylylidene))bis(4-chlorophenol)	-CH <sub>2</sub> -	-Cl
	3	2,2'-((((methylenebis(oxy))bis(methylene))bis(2,1-phenylene))bis(azanylylidene))bis(methanylylidene))diphenol	-CH <sub>2</sub> OCH <sub>2</sub> -	-H
	4	2,2'-((((methylenebis(oxy))bis(methylene))bis(2,1-phenylene))bis(azanylylidene))bis(methanylylidene))bis(4-chlorophenol)	-CH <sub>2</sub> OCH <sub>2</sub> -	-Cl
	5	2,2'-((((methylenebis(oxy))bis(methylene))bis(2,1-phenylene))bis(azanylylidene))bis(methanylylidene))bis(4-bromophenol)	-CH <sub>2</sub> OCH <sub>2</sub> -	-Br
	6	2,2'-((((ethane-1,2-diylbis(oxy))bis(methylene))bis(2,1-phenylene))bis(azanylylidene))bis(methanylylidene))diphenol	-CH <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> OCH <sub>2</sub> -	-H
	7	2,2'-((((ethane-1,2-diylbis(oxy))bis(methylene))bis(2,1-phenylene))bis(azanylylidene))bis(methanylylidene))bis(4-chlorophenol)	-CH <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> OCH <sub>2</sub> -	-Cl
	8	2,2'-((((ethane-1,2-diylbis(oxy))bis(methylene))bis(2,1-phenylene))bis(azanylylidene))bis(methanylylidene))bis(4-bromophenol)	-CH <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> OCH <sub>2</sub> -	-Br

### 2.3. The general procedure for the determination of acidic dissociation constants

A stock solution of the investigated compound was prepared by dissolving the compound (about 10 or 20 mg; about  $10^{-3}$  -  $10^{-4}$  M) in ethanol the strength of which we knew (100 mL) in a volumetric flask. Aliquots (about 1 mL) of this solution were transferred into a 10 mL volumetric flask (ethanol: acid or basic solution; 1 mL:9 mL ratios) and diluted to the mark solutions (the  $H_2SO_4$  solutions or the NaOH solutions or *pH* buffer solutions). The *pH* or  $H_0$  or  $H_-$  values were measured before and after the addition of the new solution. The absorbency of

each solution was then measured in 1 cm cells, against solvent blanks, using a constant temperature cell-holder Perkin Elmer Lambda UV35 scanning spectrometer was thermostatted at 25 °C (within  $\pm 0.1$  °C). The wavelengths were chosen so that the fully cationic or anionic form of the substrate had a much greater or a much smaller extinction coefficient compared to the neutral form. The analytical wavelengths, the half protonation values, and the UV absorption maximums for each substrate studied are shown in Tables 2 and 3. The UV-Visible spectrums of the compound 7 to different media are given in Figure 1 [22].

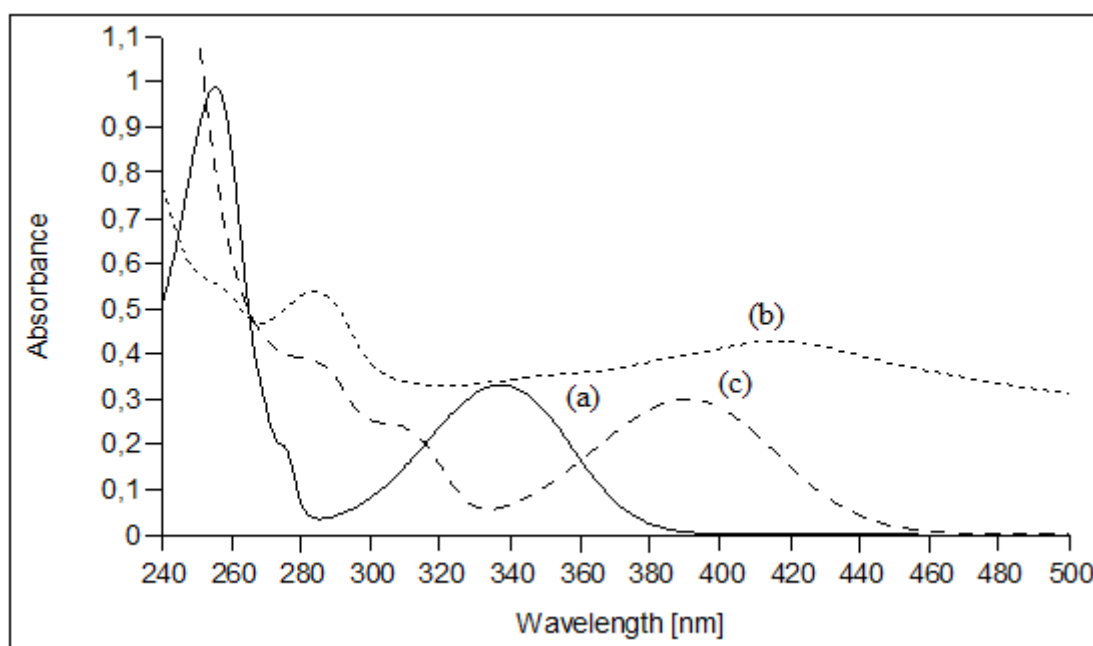


Figure 1. UV-Visible spectrum of compound 7. (a) *pH*=1; (b) *pH*= 7; (c); *pH* = 13.

The determined of acidity constant was studied by our group using a spectrophotometric method [22] and they have been published [38-46].

### 2.4. The calculation of half protonation values

The sigmoid curve of absorbency or extinction coefficients at the analytical wavelength ( $A$ ,  $\lambda$ ) was obtained in Figure 2.

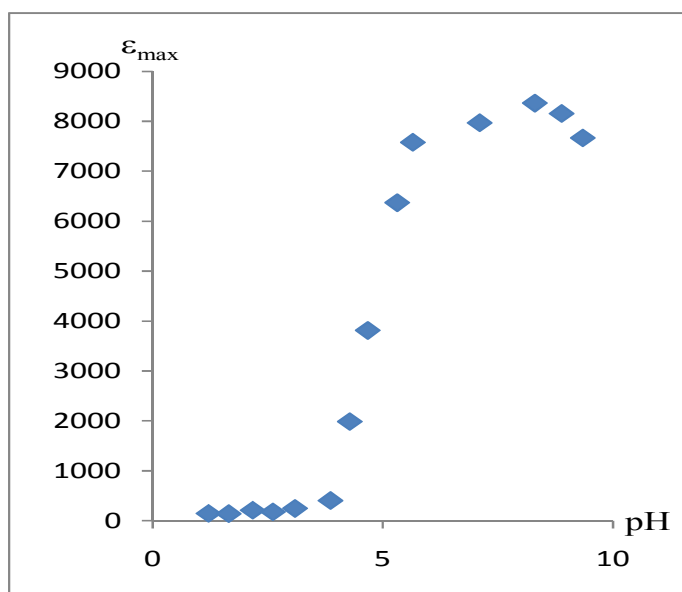


Figure 2.  $\epsilon_{\max}$  as a function of  $pH$  (390.0 nm) plot of molecule 7 for the first protonation.

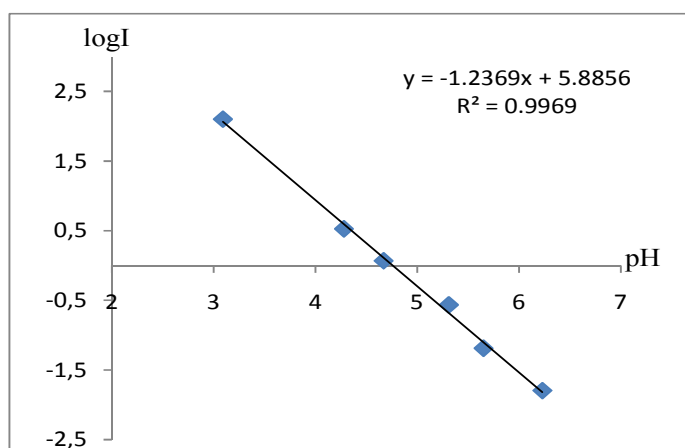


Figure 3.  $pH$  as a function of  $\log I$  (390.0 nm) plot of molecule 7 for the first protonation.

The absorbency of the fully protonated molecule ( $A_{ca}$ , absorbance of conjugated acid) and the pure free base ( $A_{fb}$ , absorbency of the free base) at an acidity were then calculated by linear extrapolation of the arms of the curve. Eq. 15 provides the ionization ratio where the  $A_{obs}$  (the observed absorbency) was in turn converted into molar extinction  $\epsilon_{obs}$  using Beers law of  $A = \epsilon bc$  ( $b$  = cell width, cm;  $c$  = concentration, mol.  $\text{dm}^{-3}$ ) [22]:

$$I = \frac{[BH^+]}{[B]} = \frac{(A_{obs} - A_{fb})}{(A_{ca} - A_{obs})} = \frac{(\epsilon_{obs} - \epsilon_{fb})}{(\epsilon_{ca} - \epsilon_{obs})} \quad (15)$$

The linear plot of  $\log I$  against  $pH$ , using the values  $-1.0 < \log I < 1.0$ , had the slope  $m$ , yielding half the protonation value of  $H_0^{1/2}$  ( $H_-^{1/2}$  or  $pH^{1/2}$  at  $\log I = 0$  in Figure 3). The  $pK_a$  values were calculated using Eq. (14).

### 3. RESULT AND DISCUSSION

A major difficulty in obtaining reliable acidity constant ( $pK_a$ ) values for the symmetry of certain Schiff bases molecules is due to their low solubility and possible hydrolysis in aqueous solutions. Therefore, it is necessary to work at low concentrations and the  $pH$  values should be neither too low nor too high. This poses limitations to the choice of method. The spectrophotometric method seems to be the most convenient. Due to the spectrophotometric method it is possible to measure the acidity constant in the aqueous phase. For this reason researchers tend to prefer this method.

The names and possible protonation patterns of the studied compounds **1-8** were depicted in Table 1 and in Schemes 1 and 2, respectively. The UV-Visible data along with the calculated acidity constants for the deprotonation and protonation processes are shown in Tables 2 and 3.

Table 2. UV-Vis. spectral data and acidity constants ( $pK_a$ ) of compounds **1-8** for deprotonation (or phenolate protonation) process

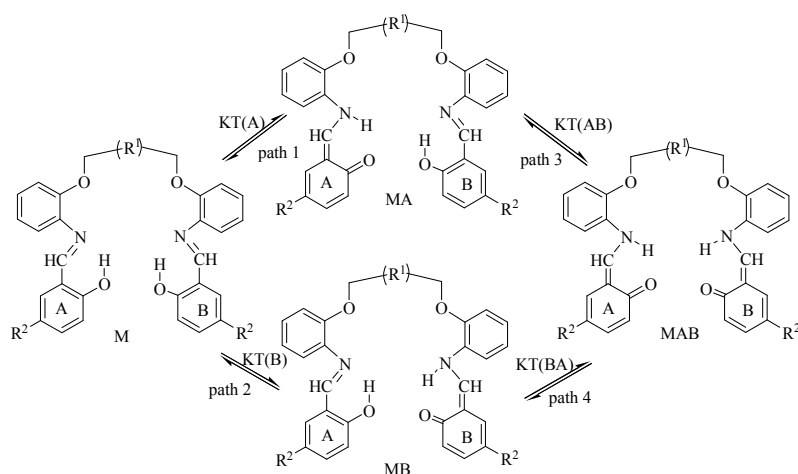
Compound	Spectral maximum $\lambda$ /nm		Acidity measurements																																																																								
	Neutral <sup>a</sup> species $\epsilon_{\max}$ (log $\epsilon_{\max}$ )	Monoanion <sup>b</sup> $\epsilon_{\max}$ (log $\epsilon_{\max}$ )	$\lambda_{\max}$ (nm) <sup>c</sup>	H <sup>1/2d</sup>	m <sup>e</sup>	$pK_a^f$	Corr. <sup>g</sup>																																																																				
<b>1</b>	358.98 (4.20)	378.63 (3.97)	378	10.587±0.24	1.352	14.316	0.920																																																																				
	279.82 (4.23)	268.63 (4.11)						<b>2</b>	390.31 (3.62)	389.82 (3.81)	337	10.256±0.16	0.849	8.707	0.993	283.72 (3.72)	283.72 (3.92)	<b>3</b>	403.45 (3.95)	378.63 (3.94)	325	10.297±0.08	4.736	48.767	0.999	282.74 (4.03)	270.09 (4.10)	<b>4</b>	412.21 (4.00)	390.31 (3.76)	390	10.804±0.09	0.631	6.817	0.993	283.72 (4.06)	284.69 (3.86)	<b>5</b>	411.73 (4.02)	390.31(3.76)	390	9.088±0.13	0.736	6.689	0.990	283.72 (4.06)	284.69 (3.89)	<b>6</b>	402.96 (3.82)	379.12 (3.90)	378	10.243±0.08	0.366	3.749	0.994	327.52 (3.88)	269.12 (4.06)	282.74 (3.96)		<b>7</b>	415.62 (3.93)	390.31 (3.78)	390	10.692±0.12	0.585	6.255	0.992	284.2 (4.04)	284.20 (3.89)	<b>8</b>	405.4 (3.93)	378.63 (4.03)	378	9.848±0.01	1.086
<b>2</b>	390.31 (3.62)	389.82 (3.81)	337	10.256±0.16	0.849	8.707	0.993																																																																				
	283.72 (3.72)	283.72 (3.92)						<b>3</b>	403.45 (3.95)	378.63 (3.94)	325	10.297±0.08	4.736	48.767	0.999	282.74 (4.03)	270.09 (4.10)	<b>4</b>	412.21 (4.00)	390.31 (3.76)	390	10.804±0.09	0.631	6.817	0.993	283.72 (4.06)	284.69 (3.86)	<b>5</b>	411.73 (4.02)	390.31(3.76)	390	9.088±0.13	0.736	6.689	0.990	283.72 (4.06)	284.69 (3.89)	<b>6</b>	402.96 (3.82)	379.12 (3.90)	378	10.243±0.08	0.366	3.749	0.994	327.52 (3.88)	269.12 (4.06)		282.74 (3.96)							<b>7</b>	415.62 (3.93)	390.31 (3.78)	390	10.692±0.12	0.585	6.255	0.992	284.2 (4.04)	284.20 (3.89)	<b>8</b>	405.4 (3.93)	378.63 (4.03)	378		9.848±0.01	1.086			
<b>3</b>	403.45 (3.95)	378.63 (3.94)	325	10.297±0.08	4.736	48.767	0.999																																																																				
	282.74 (4.03)	270.09 (4.10)						<b>4</b>	412.21 (4.00)	390.31 (3.76)	390	10.804±0.09	0.631	6.817	0.993	283.72 (4.06)	284.69 (3.86)	<b>5</b>	411.73 (4.02)	390.31(3.76)	390	9.088±0.13	0.736	6.689	0.990	283.72 (4.06)	284.69 (3.89)	<b>6</b>	402.96 (3.82)	379.12 (3.90)	378	10.243±0.08	0.366	3.749	0.994	327.52 (3.88)	269.12 (4.06)		282.74 (3.96)							<b>7</b>	415.62 (3.93)	390.31 (3.78)	390	10.692±0.12	0.585	6.255	0.992	284.2 (4.04)	284.20 (3.89)	<b>8</b>	405.4 (3.93)	378.63 (4.03)	378	9.848±0.01	1.086	10.695	0.984	328.98 (4.02)	269.12 (4.20)		282.26 (4.10)								
<b>4</b>	412.21 (4.00)	390.31 (3.76)	390	10.804±0.09	0.631	6.817	0.993																																																																				
	283.72 (4.06)	284.69 (3.86)						<b>5</b>	411.73 (4.02)	390.31(3.76)	390	9.088±0.13	0.736	6.689	0.990	283.72 (4.06)	284.69 (3.89)	<b>6</b>	402.96 (3.82)	379.12 (3.90)	378	10.243±0.08	0.366	3.749	0.994	327.52 (3.88)	269.12 (4.06)		282.74 (3.96)							<b>7</b>	415.62 (3.93)	390.31 (3.78)	390	10.692±0.12	0.585	6.255	0.992	284.2 (4.04)	284.20 (3.89)	<b>8</b>	405.4 (3.93)	378.63 (4.03)	378	9.848±0.01	1.086	10.695	0.984	328.98 (4.02)	269.12 (4.20)		282.26 (4.10)																		
<b>5</b>	411.73 (4.02)	390.31(3.76)	390	9.088±0.13	0.736	6.689	0.990																																																																				
	283.72 (4.06)	284.69 (3.89)						<b>6</b>	402.96 (3.82)	379.12 (3.90)	378	10.243±0.08	0.366	3.749	0.994	327.52 (3.88)	269.12 (4.06)		282.74 (3.96)							<b>7</b>	415.62 (3.93)	390.31 (3.78)	390	10.692±0.12	0.585	6.255	0.992	284.2 (4.04)	284.20 (3.89)	<b>8</b>	405.4 (3.93)	378.63 (4.03)	378	9.848±0.01	1.086	10.695	0.984	328.98 (4.02)	269.12 (4.20)		282.26 (4.10)																												
<b>6</b>	402.96 (3.82)	379.12 (3.90)	378	10.243±0.08	0.366	3.749	0.994																																																																				
	327.52 (3.88)	269.12 (4.06)																																																																									
	282.74 (3.96)																																																																										
<b>7</b>	415.62 (3.93)	390.31 (3.78)	390	10.692±0.12	0.585	6.255	0.992																																																																				
	284.2 (4.04)	284.20 (3.89)																																																																									
<b>8</b>	405.4 (3.93)	378.63 (4.03)	378	9.848±0.01	1.086	10.695	0.984																																																																				
	328.98 (4.02)	269.12 (4.20)																																																																									
	282.26 (4.10)																																																																										

<sup>a</sup>Measured in  $pH = 7$  buffer. <sup>b</sup>Measured in  $pH = 14$  buffer. <sup>c</sup>The wavelength for  $pK_a$  determination. <sup>d</sup>Half protonation value  $\pm$  uncertainties refer to the standard error. <sup>e</sup>Slopes for log  $I$  as a function of  $pH$  graph. <sup>f</sup>Acidity constant value for the deprotonation. <sup>g</sup>Correlations for log  $I$  as a function of the  $pH$  graph.

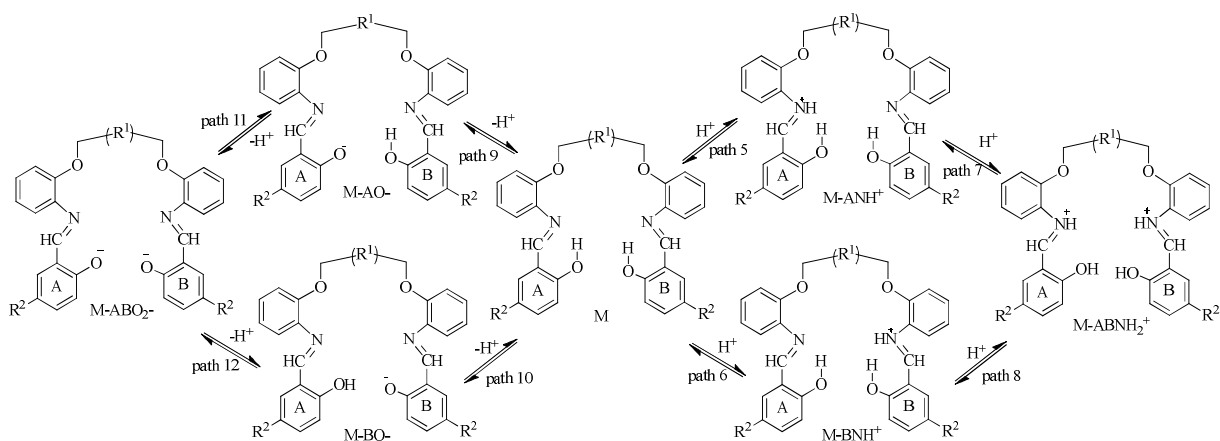
Table 3. UV-Vis. spectral data and acidity constants ( $pK_{a1}$ ,  $pK_{a2}$ ) of compounds **1-8** for the first and second protonation

Comp.	Spectral maximum $\lambda$ /nm			Acidity measurements					
	Neutral <sup>a</sup> species	Monocation <sup>b</sup>	Dication <sup>c</sup>	$\lambda^d$ /nm	$H^{1/2}(pH^{1/2})^e$	$m^f$	$pK_{a1}^g$	$pK_{a2}^h$	Corr. <sup>i</sup>
	$\epsilon_{\max}$ (log $\epsilon_{\max}$ )	$\epsilon_{\max}$ (log $\epsilon_{\max}$ )	$\epsilon_{\max}$ (log $\epsilon_{\max}$ )						
<b>1</b>	358.98 (4.20)	324.60 (3.83)		325	5.288±0.10	0.611	3.231		0.993
	279.82 (4.23)	255.97 (4.41)							
		324.6 (3.83)	393.23 (4.34)	360	-4.111±0.21	0.678		-2.787	0.990
<b>2</b>	390.31 (3.62)	337.74 (3.82)		337	3.432±0.18	1.060	3.638		0.990
	283.72 (3.72)	255.49 (4.30)							
		337.74 (3.82)	414.65 (4.21)	390	-5.384±0.17	0.519		-2.890	0.991
<b>3</b>	403.45 (3.95)	324.60 (3.83)		375	6.452±0.12	1.119	7.220		0.992
	282.74 (4.03)	256.46 (4.42)							
		324.60 (3.83)	394.26(4.28)	375	-3.212±0.16	0.400		-1.286	0.994
<b>4</b>	412.21 (4.00)	337.26 (3.80)		390	4.995±0.03	0.994	4.965		0.999
	283.72 (4.06)	255.42 (4.26)							
		337.26 (3.80)	412.21 (4.14)	336	-4.518±0.08	0.324		-1.4653	0.995
<b>5</b>	411.73 (4.02)	337.74 (3.78)		390	4.207±0.04	0.850	3.576		0.999
	283.72 (4.06)	255.97 (4.26)							
		337.74 (3.78)	414.65(4.11)	390	-5.028±0.23	0.536		-2.695	0.987
<b>6</b>	402.96 (3.82)	324.6 (3.81)		378	5.606±0.17	1.364	7.646		0.992
	327.52 (3.88)	255.97 (4.40)							
		324.6 (3.81)	392.26 (3.89)	378	-3.866±0.15	0.404		-1.562	0.992
<b>7</b>	415.62 (3.93)	337.26 (3.83)		390	4.758±0.06	1.237	5.886		0.997
	284.20(4.04)	255.97 (4.30)							
		337.26 (3.83)	413.67 (4.14)	390	-4.775±0.16	1.112		-5.310	0.998
<b>8</b>	405.40 (3.93)	325.09 (3.93)		324	4.612±0.12	0.198	0.913		0.983
	328.98 (4.02)	256.46 (4.53)							
		325.09 (3.93)	391.77 (4.35)	378	-5.165±0.77	0.503		-2.598	0.910
	256.46 (4.53)	292.96 (4.56)							

<sup>a</sup>Measured in  $pH = 7$  buffer solution. <sup>b</sup>Measured in  $pH = 1$  buffer solution. <sup>c</sup>Measured in 98 %  $H_2SO_4$ . <sup>d</sup>The wavelength for  $pK_a$  determination. <sup>e</sup>Half protonation value (uncertainties refer to the standard error). <sup>f</sup>Slopes for log I as a function of  $pH$  (or acidity function  $H_0$ ) graph. <sup>g</sup>Acidity constant value for the first protonation. <sup>h</sup>Acidity constant value for the second protonation. <sup>i</sup>Correlations for log I as a function of  $pH$  (or  $H_0$ ) graph.



Scheme 1. Possible tautomer structure for studied molecules 1-8.

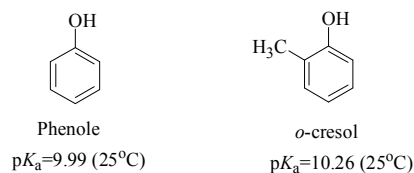


Scheme 2. Possible protonation pattern for studied molecules 1-8.

### 3.1. Deprotonation ( $pK_a$ )

All molecules have two phenolic -OH groups (A or B ring) which are symmetrical. The structure of the A and B groups, and the acidity of the phenolic-OH groups are the same. The first deprotonation of the two (A or B ring) phenolic-OH protons has taken place in each one as shown in Scheme 2. We can consider this the first deprotonation taking into account the similarity of the phenol and *o*-cresol ionization. The variation of the deprotonation depends on the substituents on the phenolic ring (A or B). While electron-donating substituents increase the basicity they also decrease the acidity. We believe that the first deprotonation takes place in the strongly basic region by the removal of protonation from the -OH group of the phenolic ring which corresponds to the electron-donating substituents at the *o*-CH<sub>3</sub> group ( $\sigma_{o-CH_3}=0.19$ ) [47] decreasing the acid dissociation constants.

The studied compounds 1-8 have been edited as shown in Figure 4.

Figure 4. Acidity of phenol [48] and *o*-cresol [49].

They are similar to a pair of *o*-cresol as can be seen in Figure 4. Phenol-**S<sub>B</sub>** (**S<sub>A</sub>**)-phenol, **S<sub>A</sub>** or **S<sub>B</sub>** corresponds to substituent electron-withdrawing or electron-donating when the acidity values are increased or reduced by the effects of phenolic-OH protons. For this reason, we can say that all  $pK_a$  values change because of this neighboring group participation, as shown in Figure 5.



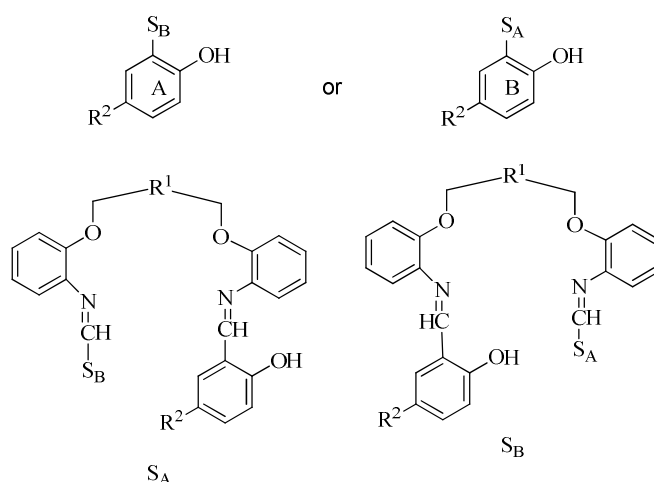


Figure 5. General structures are shown for studied compounds.

When we put the molecules in an increasing basicity order for the first deprotonation ( $pK_a$ ), the following trend is obtained;

<b>Molecule:</b>	<b>5</b>	<b>8</b>	<b>6</b>	<b>2</b>	<b>3</b>	<b>1</b>	<b>7</b>	<b>4</b>
$pK_a$ :	9.088	> 9.848	> 10.243	> 10.256	> 10.297	> 10.587	> 10.692	> 10.804
								increasing basicity

The most acidic or the least basic molecule seems to be molecule 5. In fact, molecule 5 has a  $pK_a$  value within this slightly basic region. Molecule 4 gives a proton in the strongly basic region and it becomes the least acidic. Molecules 1-2, 3-5 and 6-8 have a similar structure, so it would be better to compare these molecules (Table 2).

Molecule 1 is more basic than molecule 2 cause of the electron-withdrawing effect of the chlorine atom on the phenolic ring ( $\sigma_{p-Cl}=0.227$ ) [47]. So, the electron-withdrawing effect of the substitute chloride atom increases the acidity of the phenolic ring, therefore this molecule can give the proton in the least basic region.

We can easily see that molecule 5 is more acidic than molecules 3 and 4 for the first deprotonation, and when we rearrange them in an increasing acidity order: Molecule 5; 9.088 ( $\sigma_{p-Br}=0.232$ ) molecule 3; 10.297 ( $\sigma_{p-H}=0$ ), molecule 4; 10.804 ( $\sigma_{p-Cl}=0,227$ ) [47]. Molecule 4 is more basic than molecule 5 because of the electron-withdrawing effect of the chlorine atom of the *o*- $S_A$  (or  $S_B$ ) group. We can consider as the first deprotonation taking into account the similar structure of molecules 6, 7 and 8 and when we rearrange them in an increasing acidity order, we get the following trend:

Molecule 8; 9.848 ( $\sigma_{p-Br}=0.232$ ), molecule 6; 10.243 ( $\sigma_{p-H}=0$ ), molecule 7; 10.692 ( $\sigma_{p-Cl}=0,227$ ).

<b>Molecule:</b>	<b>2</b>	<b>5</b>	<b>8</b>	<b>7</b>	<b>4</b>	<b>1</b>	<b>6</b>	<b>3</b>
$pK_{a1}$ :	3.432	> 4.207	> 4.612	> 4.758	> 4.995	> 5.288	> 5.606	> 6.452
								decreasing acidity

In the present study, we report the experimental acid dissociation of the first deprotonation acidity constant values of certain symmetrically Schiff bases on phenolic-OH. We were expecting the second deprotonation in the super-basic (1N-10N KOH), but the second deprotonation could not be measured experimentally.

### 3.2. The first protonation ( $pK_{a1}$ )

The UV-Visible spectral and protonation data of the studied compounds 1-8 are shown in Table 3, with possible protonation patterns shown in Scheme 2. The first protonation in the pH of the acidic region (pH= 7-1), and the second protonation in the super acidic region (1-98%  $H_2SO_4$ ) were investigated.

In molecules with similar features for the first protonation, constant acidity would be more correct to interpret. The studied compounds are shown in Figure 6, which is a symmetrical first neighboring  $-CH=N-$  protonation of the phenolic A ring nitrogen atom (or a phenolic ring B adjacent  $-CH=N-$  group) results from any of the nitrogen atoms. Electron-withdrawing groups reduce the electron density of the nitrogen at the imine group and the nitrogen basicity strength is therefore reduced. According to the explanations above the order of first protonation can be written as follows:

The first protonation ( $pK_{a1}$ );

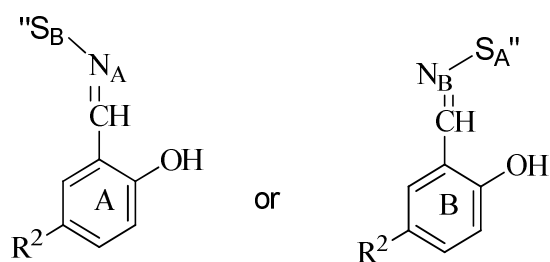


Figure 6. The first acidity structures are shown for studied compounds.

This order of decreasing acidity seems logical considering the strong electron-withdrawing effects of the substituent  $R^2$ . The molecules are symmetrical, which protonated the nitrogen atoms from  $N_A$  or  $N_B$ . The increase or the decrease in the basicity on the nitrogen atom is due to the  $R^2$  substituent and the group of  $S_{A'}$  or  $S_{B'}$ . This explanation of the acidity constant would be better tested among similar molecules.

Molecule 2 is the least basic with protonation taking place in the strong acid region. Molecule 3 is the most basic with protonation taking place in the weak acidic region. Due to the effects of  $S_{A'}$  and  $S_{B'}$ , molecule 1 is found in the ring A (or B)  $p$ -H at  $R^2$  less than the acidic molecule is found in the substituent of  $p$ -Cl at  $R^2$ . This makes the ionization process easier. However, the mechanism of the first protonation of molecules 3, 4 and 5 remains the same. In molecule 3, there is no substituent at  $R^2$  which means that no effective group exists on the atom to change the acidity of the molecule. Therefore, it is more basic than molecules 4 and 5. The strongly electron-withdrawing effect of the  $\sigma_{p-Br}$  substituent caused an increase of the  $pK_a$  value of the molecule for the first protonation as expected. This situation is shown below as:

Molecule 5; 4.207 ( $\sigma_{p-Br}=0.232$ ), molecule 4; 4.995 ( $\sigma_{p-Cl}=0.227$ ); molecule 3; 6.452 ( $\sigma_{p-H}=0$ ).

In this way, the groups at  $S_B$  and  $S_{A'}$  withdraw electrons from the ring at A (or B) and make protonation possible for the group of  $N_B$  (or  $N_B$ ) as shown in Figure 6. For molecules 6, 7 and 8, we can easily see that these molecules have a similar structure, as shown below:

Molecule 8; 4.612 ( $\sigma_{p-Br}=0.232$ ), molecule 7; 4.758 ( $\sigma_{p-Cl}=0.227$ ); molecule 6; 5.606 ( $\sigma_{p-H}=0$ ).

Molecule 6 becomes less acidic because it has no electron-withdrawing group. Molecule 8 is more acidic than molecule 7 because of the electron-withdrawing effect of the bromine atom on ring A (or B). Moreover, the strong electron-withdrawing effect of the  $\sigma_{p-Br}$  substituent caused an increase in the  $pK_{a1}$  values of molecule 8.

### 3.3. The second protonation ( $pK_{a2}$ )

We believe that the second protonation takes place at  $N_A$  or  $N_B$  as shown in Figure 7, the structure of the molecule for the second protonation.

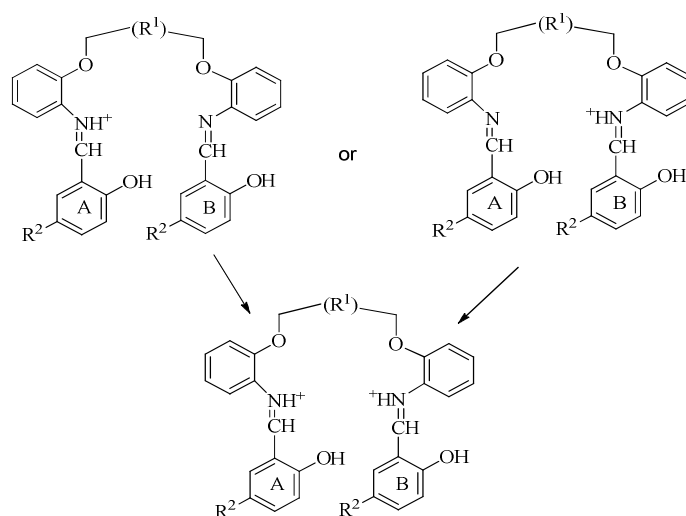


Figure 7. Studied compounds in general of the second protonation.

The  $pK_{a2}$  of all the molecules (1 to 8) is found to be associated with the protonation of the imine nitrogen atom. The first protonation of the protonated nitrogen atom acted as an electron-withdrawing group ( $S_A'''$  or  $S_B'''$ ), for the second protonation in Figure 8. The second protonation came from the  $S_A'''$  (or  $S_B'''$ ) group of the electron-withdrawing from the unprotonated nitrogen

atom, and also from the  $R^2$  electron-withdrawing molecules. So, this nitrogen atom, in the presence of a strongly acidic region, is protonated in Table 3. The acidity constant values ( $pK_{a2}$ ) are obtained, and for this region can be arranged in the decreasing acidity order as shown below:

<b>Molecule:</b>	<b>2</b>	<b>8</b>	<b>5</b>	<b>7</b>	<b>4</b>	<b>1</b>	<b>6</b>	<b>3</b>
$pK_{a2}$ :	-5.384	> -5.165	> -5.028	> -4.775	> -4.518	> -4.111	> -3.866	> -3.212

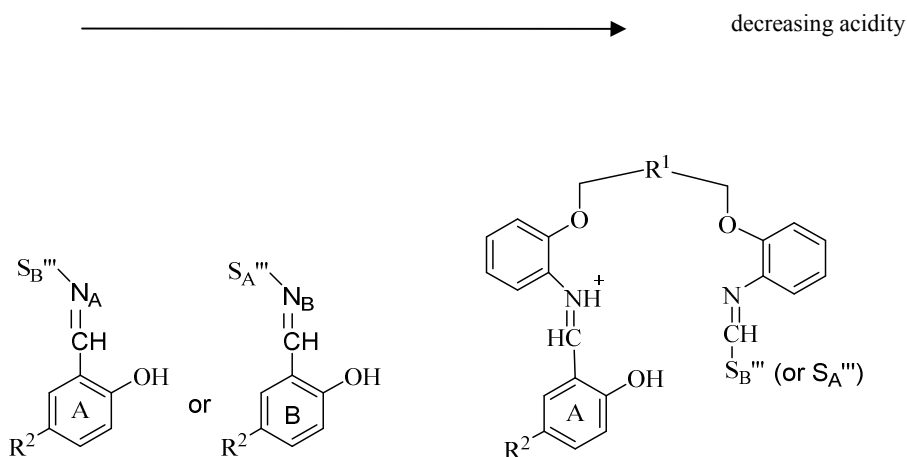


Figure 8. Studied compounds of the second acidity structures.

This order of decreasing acidity seems logical for the second protonation as it is for the first protonation. Molecule 2 ( $pK_{a2}$ : -5.384  $\sigma_{p-Cl}$ =0.227) is more acidic than molecule 1 ( $pK_{a2}$ : -4.111 ( $\sigma_{p-H}$ =0)). For molecule 2, the second protonation occurs within the strongly acidic region. Molecule 1 has one electron-withdrawing  $S_A'''$  (or  $S_B'''$ ) group, but molecule 2 has both of the electron-withdrawing groups  $S_A'''$  (or  $S_B'''$ ) located at the  $p$ -Cl at  $R^2$ , due to its decreasing basicity. The protonation of molecule 2 seems to take place in the strongly acidic region.

The electron-withdrawing order goes as follows: Molecules 3, 4 and 5 respectively. This order has a parallelism depending on the substituent constant as shown below:

Molecule 3; -3.212 ( $\sigma_{p-H}$ =0), molecule 4; -4.518 ( $\sigma_{p-Cl}$ =0.227); molecule 5; -5.028 ( $\sigma_{p-Br}$ =0.232).

It seems that the second protonation of molecules 6, 7 and 8 occurs with a mechanism similar to that shown in Figure 8, due to similar structures. The most acidic or the least basic molecule seems to be molecule 8. In fact, the strongly electron-withdrawing group was the bromide depending on its substituent constant as shown below:

Molecule 6; -3.866 ( $\sigma_{p-H}$ =0), molecule 7; -4.775 ( $\sigma_{p-Cl}$ =0.227); molecule 8; -5.165 ( $\sigma_{p-Br}$ =0.232).

#### 4. CONCLUSIONS

The acidity constants of symmetric Schiff bases were calculated using an UV-vis. spectrophotometric method at a temperature of 25 ( $\pm 0.1$ ) °C. The deprotonated acidity constants ( $pK_a$ ) have been found to be associated with the deprotonation of phenolate oxygen. The first and second protonated acidity constants ( $pK_{a1}$  and  $pK_{a2}$ ) have been found to cause the protonation of the imine nitrogen atom for all molecules. The deprotonation acidity constants ( $pK_a$ ) were found for molecule 5 (9.088), molecule 8 (9.848), molecule 6: (10.243), molecule 2 (10.256), molecule 3 (10.297), molecule 1 (10.587), molecule 7 (10.692) and molecule 4 (10.804). The first protonation ( $pK_{a1}$ ) was found molecule 2: 3.432, molecule 5: 4.207, molecule 8: 4.612, molecule 7: 4.758, molecule 4: 4.995, molecule 1: 5.288, molecule 6: 5.606 and molecule 3: 6.452. The second protonation ( $pK_{a2}$ ) was found molecule 2: -5.384, molecule 8: -5.165, molecule 5: -5.028, molecule 7: -4.775, molecule 4: -4.518, molecule 1: -4.111, molecule 6: -3.866 and molecule 3: -3.212.

#### ACKNOWLEDGEMENT

This article is dedicated to the memory of our colleague Prof. Dr. Cemil Öğretir who passed away on January 19, 2011.

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

## REFERENCES

- [1] Calligaris, M., Randaccio, L., *In Comprehensive Coordination Chemistry*, Wilkinson, G., Ed.; Pergamon: London, Vol. 2, p 715, (1987).
- [2] Jia, H.P., Li, W., Ju, Z.F., Zhang, J., "Synthesis, Structure, and Magnetic Properties of a Novel Mixed-Bridged Heterometal Tetranuclear Complex  $[Mn_2Ni_2(MeOSalen)_2(11,1-N_3)_2(N_3)_2]$ ", *Inorg. Chem. Commun.*, 10: 397-400 (2007).
- [3] Cohen, M.D., Schmidt, G.M.J., Flavian, S., "Topochemistry. VI. Experiments on Photochromy and Thermochromy of Crystalline Anils of Salicylaldehydes", *J. Chem. Soc.*, 2041-2051 (1964).
- [4] Lahav, M., Schmidt, G.M.J., "Topochemistry. XXIII. The Solidstate Photochemistry at 25 Deg of Some Muconic Acid Derivatives", *J. Chem. Soc. B*, 312-317, (1967).
- [5] Hadjoudis, E., Vitterakis, M., Moustakali-Mavridis, I., "Photochromism and Thermochromism of Schiff Bases in the Solid and in Rigid Glasses", *Tetrahedron*, 43: 1345-1360 (1987).
- [6] Kaya, I., Yıldırım, M., Avci, A., "Synthesis and Characterization of Fluorescent Polyphenol Species Derived From Methyl Substituted Aminopyridine Based Schiff Bases: The Effect of Substituent Position on Optical, Electrical, Electrochemical, and Fluorescence Properties", *Synth. Met.*, 160: 911-920 (2010).
- [7] Ramakrishna, D., Bhat, B.R., Karvembu, R., "Catalytic Oxidation of Alcohols by Nickel (II) Schiff Base Complexes Containing Triphenylphosphine in Ionic Liquid: an Attempt towards Green Oxidation Process", *Catal. Commun.*, 11: 498-501 (2010).
- [8] Soltani, N., Behpour, M., Ghoreishi, S. M., Naeimi H., "Corrosion Inhibition of Mild Steel in Hydrochloric Acid Solution by Some Double Schiff Bases", *Corr. Sci.*, 52: 1351-1361 (2010).
- [9] Sabaa, M.W., Mohamed, R.R., Oraby, E.H., "Vanillin-Schiff's Bases as Organic Thermal Stabilizers and Co-stabilizers for Rigid Poly(vinyl chloride)", *Europ. Poly. J.*, 45: 3072-3080 (2009).
- [10] Chakraborty, A., Kumar, P., Ghosh, K., Roy, P., "Evaluation of a Schiff Base Copper Complex Compound as Potent Anticancer Molecule with Multiple Targets of Action", *Europ. J. Pharm.*, 647: 1-12 (2010).
- [11] Kamel, M. M., Ali, H. I., Anwar, M.M., Mohamed, N.A. Soliman, A.M., "Synthesis, Antitumor Activity and Molecular Docking Study of Novel Sulfonamide-Schiff's Bases, Thiazolidinones, Benzothiazinones and Their c-nucleoside Derivatives", *Europ. J. Medic. Chem.*, 45: 572-580 (2010).
- [12] Roswadowski, Z., Majewski, E., Dziembowska, T., Hansen, P.E., "Deuterium Isotope Effects On  $^{13}C$  Chemical Shifts of Intramolecularly Hydrogenbonded Schiff's Bases", *J. Chem. Soc. Perkin Trans.*, 2: 2809 (1999).
- [13] Zgierski, M.Z., "Theoretical Study of Photochromism of N-salicylidene-R-benzylamine", *J. Chem. Phys.*, 115: 8351 (2001).
- [14] Filarowski, A., Koll, A., Glowiak, T., Majewski, E., Dziembowska, T., "Proton-transfer Reaction in N-methyl-2-hydroxy Schiff Bases", *Ber. Bunsen-Ges. Phys. Chem.*, 97: 393 (1993).
- [15] Koll, A., Rospenk, M., Jagodzinska, E., Dziembowska, T., "Dipole Moments and Conformation of Schiff Bases with Intramolecular Hydrogen Bonds", *J. Mol. Struct.*, 552: 193-204 (2000).
- [16] Gilli, P., Ferretti, V., Bertolasi, V., Gilli, G., *A Novel Approach to Hydrogen Bonding Theory In Advances in Molecular Structure Research*, Hargittai, M., Hargittai, I., Eds.; JAI Press: Greenwich, CT, Vol. 2, p 667 (1996).
- [17] Niazi, A., Zolgharnein, J., Davoodabadi, M.R., "Spectrophotometric Determination of Acidity Constant of Some Indicators in Various Micellar Media Solutions by Rank Annihilation Factor Analysis", *Spectrochim. Acta A*, 70: 343-349 (2008).
- [18] Dumanovic, D., Juranic, I., Dzeletovic, D., Vasic, V.M., Jovanovic, J., "Protolytic Constants of Nizatidine, Ranitidine and N,N'-dimethyl-2-nitro-1,1-ethenediamine; Spectrophotometric and Theoretical Investigation", *J. Pharm. Biomed. Anal.*, 15: 1667-1678 (1997).
- [19] Frey, P.A., Kokesh, F.O., Westheimer, F.H., "A Reporter Group at the Active Site of Acetoacetate Decarboxylase Ionization Constant of the Nitrophenol", *J. Am. Chem. Soc.*, 93: 7266-7270 (1971).
- [20] Türkoğlu, G., Berber H., Dal, H., Öğretir, C., "Synthesis, characterization, tautomerism and theoretical study of some new Schiff base derivatives", *Spectroc. Acta Part A.*, 79, 1573- 1583 (2011).
- [21] Türkoğlu, G., *Bazı Difenolik Schiff Bazılarının Sentezi ve Yapılarının Aydınlatılması*, Anadolu Üniversitesi, Yüksek Lisans Tezi, Kimya Anabilim Dalı, Eskişehir, (2007).

- [22] Albert, A., Serjeant, E.P., *The Determination of Ionisation Constants*, Chapman and Hall London, U.K., (1971).
- [23] Wiberg, B.K., *Physical Organic Chemistry*, Wiley: New York, (1963).
- [24] Hammett, L.P., Deyrup, A.J., "A Series of Simple Basic Indicators. I. The Acidity Functions of Mixtures of Sulfuric and Perchloric Acids With Water", *J. Am. Chem. Soc.*, 54(7): 2721-2739 (1932).
- [25] Jorgenson, M.J., Hartter, D.R., "A Critical Re-evaluation of the Hammett Acidity Function at Moderate and High Acid Concentrations of Sulfuric acid New  $H_0$  Values Based Solely on a Set of Primary Aniline Indicators", *J. Am. Chem. Soc.*, 85: 878-883 (1963).
- [26] Johnson, C.D., Katritzky, A.R., Shapiro, S., "The protonation of Aromatic Carbonyl Compounds", *J. Am. Chem. Soc.*, 9: 6453-6457 (1968).
- [27] Cookson, R.F., "The Determination of Acidity Constants", *Chem. Rev.*, 74: 1 (1974).
- [28] Bowden, K., "Acidity Functions for Strongly Basic Solutions", *Chem. Rev.*, 66: 2 (1966).
- [29] Perrin, D.D., *Buffers for pH and Metal Ion Control*; Chapman and Hall: London, U.K., (1971).
- [30] Deno, N.C., Jaruzelski, J.J. "Carbonium ions. I. An acidity Function (Co) Derived from Arylcarbonium Ion Equilibriums", *J. Am. Chem. Soc.*, 77: 3044-3051 (1955).
- [31] Orloft, M.K., Fitts, D.D., "Semiempirical S.C.F.-L.C.A.O.-M.O. Treatment of Furan", *J. Chem. Phys.*, 38: 2334-2338 (1963).
- [32] Yates, K., Stevens, J.B., Katritzky, A.R., "The Ionization Behavior of Amides in Concentrated Sulfuric Acids. I. A New Acidity Function Based on a Set of Primary Amide Indicators", *Can. J. Chem.*, 42: 1957-1970 (1964).
- [33] Arnett, E.M., Mach, G.W., "Solvent Effects in Organic Chemistry. IV. The Failure of Tertiary Aromatic Amines as Hammett Bases", *J. Am. Chem. Soc.*, 86: 2671-2677 (1964).
- [34] Yates, K., McClelland, R.A., "Mechanisms of ester hydrolysis in aqueous sulfuric acids", *J. Am. Chem. Soc.*, 89(11): 2686-2692 (1967).
- [35] Schwarzenbach, G., Sulzberger, R., "The Alkalinity of Strong Solutions of the Alkali Hydroxides", *Helv. Chim. Acta*, 27: 348-362 (1944).
- [36] Rochester, C.H., *Acidity Functions*, Academic Press: London, (1970).
- [37] Jones, J.R., *The Ionization of Carbon Acids*, Academic Press: New York, (1973).
- [38] Özkütük, M., Öğretir, C., Arslan, T., Kandemirli, F., Köksoy, B., "An Experimental Study On Acid Dissociation Constants of Some Novel Isatin Thiosemicarbazone Derivatives", *J. Chem. Eng. Data*, 55: 2714-2718 (2010).
- [39] Öğretir, C., Berber, H., Asutay, O., "Spectroscopic Determination of Acid Dissociation Constants of Some Imidazole Derivatives", *J. Chem. Eng. Data*, 46: 1540-1543 (2001).
- [40] Öğretir, C., Dal, H.; Berber, H., Taktak, F.F., "Spectroscopic Determination of Acid Dissociation Constants of Some Pyridyl Schiff Bases", *J. Chem. Eng. Data*, 51: 46-50 (2006).
- [41] Berber, H., Öğretir, C., Sev Lekesiz, E.Ç., Ermis, E., "Spectroscopic Determination of Acidity Constants of Some Monoazo Resorcinol Derivatives", *J. Chem. Eng. Data*, 53: 1049-1055 (2008).
- [42] Gülseven Sıdır, Y., Sıdır, İ., Berber H., Taşal, E., Öğretir, C., "Spectroscopic Determination of Acid Dissociation Constants of Some Novel Drug Precursor 6-Acylbenzothiazolon Derivatives", *J. Chem. Eng. Data*, 55: 4752-4756 (2010).
- [43] Taktak, F.F., Berber, H., Dal, H., Öğretir, C., "Spectroscopic Determination of the Acid Dissociation Constants of Some 2-Hydroxy Schiff Base Derivatives", *J. Chem. Eng. Data*, 56: 2084-2089 (2011).
- [44] Gülseven Sıdır, Y., Sıdır, İ., Berber H., "Spectroscopic Determination of Acid Dissociation Constants of N-Substituted-6-acylbenzothiazolon Derivatives", *J. Phys. Chem. A*, 115: 5112-5117 (2011).
- [45] Öğretir, C., Görgün, K., Özkütük, M., Sakarya, H.C., "Determination and evaluation of acid dissociation constants of some novel benzothiazole Schiff bases and their reduced analogs by spectroscopy", *ARKIVOC*, vii: 197-209 (2009).
- [46] Öğretir, C., Yarılgan, S., Demirayak, Ş., "Spectroscopic Determination of Acid Dissociation Constants of Some Biologically Active 6-Phenyl-4,5-dihydro-3(2H)-pyridazinone Derivatives", *J. Chem. Eng. Data*, 47: 1396-1400 (2002).
- [47] Hansch, C., Leo, A., Taft, R.W., "A Survey of Hammett Substituent Constants and Resonance and Field Parameters", *Chem. Rev.*, 97: 165-195 (1991).
- [48] Ang, K., Tan, S., "Ionization Constants of Some Hydroxy-Pyrones at 25°C", *J. Chem. Soc. Perkin Trans.*, 2: 1525-1526 (1979).
- [49] Dean, J.A., Edited by, *Lange's Handbook of Chemistry*, (15th Edition); McGraw-Hill Mar Vol: 2, (2001).