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Solute-Solvent Interaction Effects on Protonation Equilibrium of Substituted *N*-Benzylidene-2-hydroxyanilines in Aqueous Ethanol: The Application of Factor Analysis to Solvatochromic Parameters and Protonation Equilibria

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Summary. In this study, the stoichiometric protonation constants, logK_{OH} and logK_{NH}, of sixteen substituted *N*-benzylidene-2-hydroxyanilines have been determined potentiometrically in ethanol-water mixtures of varying composition (10–80% ethanol by volume) at 25.0 ± 0.1°C. The values of the constants, log$K$, were submitted to factor analysis in order to obtain the number of factors which affect the variation of the whole data sets of protonation constants and, afterwards, to target factor analysis to identify these factors. The influence of solvatochromic parameters in the interactions between *Schiff* bases derivatives and the solvent studied was identified and quantified. *Kamlet and Taft* general equations allow calculation of the log$K$ values of Schiff bases studied in any ethanol-water mixtures up to 80% (v/v) and thus provide the knowledge of the acid-base behaviour in these solvent media. Further, the quasi-lattice quasi-chemical (QLQC) theory of preferential solvation has been applied to quantify the preferential solvation by water of electrolytes in ethanol-water mixtures.

Keywords. *Schiff* bases; Protonation constants; Solvatochromic parameters; Factor analysis; Preferential solvation.

Introduction

Many exciting and new instrumental methods require the use of organic reagents as essential components of the analytical systems to improve selectivity and sensitivity. *Schiff* bases are attractive as analytical reagents having wide applications in colorimetric titrations, ring-oven technique, and determinations of various organic and inorganic substances because they are simple and inexpensive [1]. It has been

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also observed that *Schiff* bases with C=N groups are of considerable biological importance, as they show antimicrobial activities [2] and the examination of protonation equilibria of *Schiff* bases is essential since the antimicrobial activity of *Schiff* bases is *pH*-dependent.

Push-pull substituted aromatic azomethine compounds like substituted *N*-benzylideneanilines can manifoldly interact with acids, bases, and polar solvent molecules [3–7], because both basic and acidic sites and a dipolar delocalized π-electron system are present. For this study, we chose the azomethine dye, various substituted *N*-benzylidene-2-hydroxyanilines, due to possibility of various intra- and intermolecular interactions with dipolar solvents, acids, and bases.

Among the wide range of eligible mixtures, $Et\mathrm{OH}/\mathrm{H_2O}$ on have been found especially suitable because they show simultaneously a low polar character and a partially aqueous content, as do all biological systems. Therefore, the knowledge of protonation constants of *Schiff* bases in $Et\mathrm{OH}/\mathrm{H_2O}$ mixtures is essential for improving the analytical methodology in mixed solvent systems; these are decisive for the performing of biological, pharmaceutical, and other industrial applications such as those related to chemical stability and metal-ligand stability. However, the infinite number of different solvent compositions, which can be prepared from a particular binary system, precludes determination of the log*K* values in all the compositions. Furthermore, there is an additional difficulty in obtaining the protonation constants of the *Schiff* bases in water due to their low solubility. Therefore, an equation, which connects the log*K* value of acids and bases to the solvent composition, would be very useful.

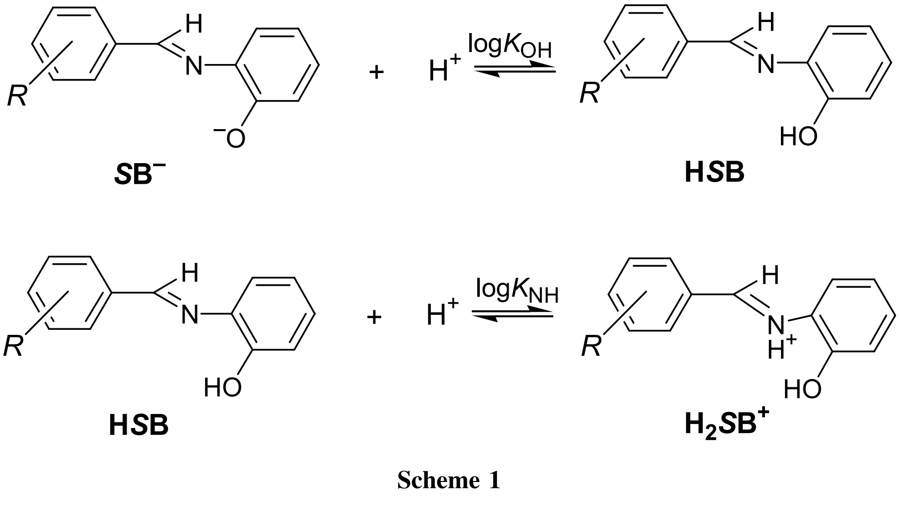
Previously, the solvent effect on the protonation equilibrium was believed to be chiefly guided by electrostatic interactions (*Born* model). But recent studies [8–11] reveal that the change in macroscopic properties such as the dielectric constant (ε) or molar fraction of solvent cannot be the sole factor. Thus, it is desirable to develop other empirical functions to take into account the complete picture of all intermolecular forces acting between solute and solvent molecules [10, 12–15].

When the studies that determine available protonation constant values of *N*-benzylidene-2-hydroxyanilines were examined, it was observed that there is neither a systematic study on the determination of the protonation constants of these *Schiff* bases in ethanol-water media nor one on the correlation between the protonation constants and the most significant solvent properties in order to determine the influence of each property on the protonation process [16, 17]. As a continuation of our extensive systematic study [18, 19] on the effect of solvent composition on the protonation constants, the purpose of the present study is the potentiometric determination of protonation constants of sixteen *Schiff* bases (H*S*B) derived from 2-hydroxyaniline with some substituted benzaldehydes in 10, 20, 30, 40, 50, 60, 70, and 80% (v/v) ethanol-water mixtures.

The variation in the log*K* values obtained and the acid-base behavior of the solutes over the whole composition range studied can be explained by taking into account the preferential solvation of ions, quantified by application of the quasi-lattice quasi-chemical, QLQC, theory [20–23]. Furthermore, the results obtained can be discussed in terms of average macroscopic and microscopic properties of the mixed solvents. There are several empirical ways to measure the effects of the solvent in water-organic co-solvent mixtures [10], one of the most ambitious and successful of which is the quantitative treatment using a multiparameter equation, also known as linear solvation energy relationship (LSER), which explains any solute property varying with solvent composition as a linear combination of the solvatochromic parameters of the solvent, π^* (solvent dipolarity/polarizability), α (solvent hydrogen-bond-donating acidity, HBD), and β (solvent hydrogen-bond-accepting basicity, HBA). These solvatochromic parameters, together with other macroscopic parameters (molar fraction, the dielectric constant (ε)) and an independent term, were tested as targets and the *Kamlet-Taft* equation appropriate (LSER, $\mathrm{XYZ} = \mathrm{XYZ_o} + \mathrm{s}\pi^* + \mathrm{a}\alpha + \mathrm{b}\beta$) [24–26] to each substance was worked out. In order to determine the number of solvent features involved in the variation of the protonation constant values of the *Schiff* bases studied in the solvent mixtures, factor analysis technique (FA) has been used. Afterwards, target factor analysis (TFA) was used to identify these factors. The equations obtained allow calculation of the log*K* values of the *Schiff* bases studied in any ethanol-water mixtures up to 80% (*v*/*v*) and thus provide the knowledge of the acid-base behavior of these important *Schiff* bases. The other practical application of these equations has been the estimation of log*K* values of *Schiff* bases sparingly soluble in water.

Results and Discussion

The stoichiometric protonation constant values were determined using the *BEST* program for the sixteen substituted *N*-benzylidene-2-hydroxyaniline *Schiff* bases (H*S*B) derived from 2-hydroxyaniline with some substituted benzaldehydes in 10, 20, 30, 40, 50, 60, 70, and 80% (*v*/*v*) ethanol-water mixtures at 25.0 ± 0.1°C. The protonation constants in water are not determined, owing to the low solubility of the *Schiff* bases in this medium. These compounds have only two proton binding sites, a phenolic group and an azomethine nitrogen group. The phenolic group is known to be weakly acidic, indicating stronger bonding between the proton and oxygen donor. This means that the proton-ligand stability constants of the ligands containing a phenolic –OH group should be high. Thus, the first protonation equilibrium refers to the protonation equilibrium of phenolate ion ($\log K_{\mathrm{OH}}$) and the



Scheme 1

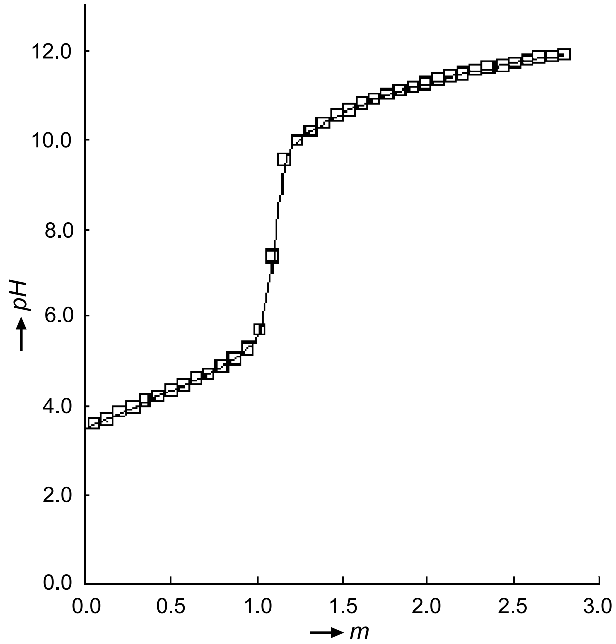


Fig. 1. Titration profile of *N*-benzylidene-2-hydroxyaniline (m = moles of base added per mol of ligand present)

second equilibrium to the protonation equilibrium of azomethine nitrogene ($\log K_{NH}$). These equilibria were shown in Scheme 1, respectively. The values of $\log K_{OH}$ and $\log K_{NH}$ for all *Schiff* bases and the titration profile in Fig. 1 show that the protonated phenolic hydrogen atom and the azomethine nitrogene atom are completely dissociable in separate steps. The values obtained for the protonation constants in all the solvent mixtures studied are reported in Table 1.

The values of the protonation constants ($\log K_{OH}$ and $\log K_{NH}$) of *Schiff* bases show that the substituent on the phenyl rings of the benzaldehyde component does not have much influence on the electron density at the phenolate oxygen and the azomethine nitrogen. Therefore, we have not observed any regularity between the $\log K$ values and the type and position of the substituents. This lack of regularity can probably be attributed to the fact that the substituents are far from the phenolate oxygen and the azomethine nitrogen [27]. This assumption was also confirmed by the plots of the protonation constants $\log K_x$ *vs.* the *Hammett* substituent constants, σ_{Ham}, for *Schiff* bases which do not conform to the *Hammett* model by showing very poor statistical results (correlation coefficients, $r^2 \leq 0.005$).

It is also interesting to compare the protonation constants of substituted *N*-benzylidene-2-hydroxyanilines with those of substituted salicylideneanilines reported in previous studies for some ethanol-water media [28]. It can be seen that both $\log K_{OH}$ and $\log K_{NH}$ values of substituted benzylideneanilines (*BA*) studied are higher than those of the corresponding salicylideneanilines (*SA*) for each ethanol-water mixture. This result can be attributed to the fact that the electron densities of nitrogen atoms and phenolate ions in the case of salicylideneanilines are smaller because of the substituents with inductive, resonance, or mesomeric effects [29, 30]. It can be imagined that these values obtained for the protonation constants of the

Table 1. Stoichiometric protonation constants for some substituted *N*-benzylidene-2-hydroxyanilines in ethanol-water mixtures at 25.0 ± 0.1°C; uncertainties in the protonation constants are ± 0.05 or lower ($\sigma_{\text{fit}} < 0.02$)

R	10% *Et*OH (0.033)[a]		20% *Et*OH (0.072)[a]		30% *Et*OH (0.117)[a]		40% *Et*OH (0.170)[a]	
	$\log K_{OH}$	$\log K_{NH}$	$\log K_{OH}$	$\log K_{NH}$	$\log K_{OH}$	$\log K_{NH}$	$\log K_{OH}$	$\log K_{NH}$
H	9.93	4.66	10.05	4.62	10.24	4.55	10.49	4.47
2-CH_3	9.89	4.68	10.05	4.62	10.25	4.53	10.46	4.45
3-CH_3	9.91	4.68	10.06	4.60	10.25	4.52	10.44	4.40
4-CH_3	9.89	4.70	10.05	4.60	10.24	4.49	10.44	4.38
2-OCH_3	9.90	4.70	10.05	4.62	10.23	4.55	10.46	4.49
4-OCH_3	9.90	4.70	10.05	4.63	10.24	4.56	10.47	4.49
3-F	9.92	4.69	10.05	4.62	10.25	4.52	10.47	4.43
4-F	9.91	4.70	10.05	4.62	10.26	4.51	10.48	4.44
2-Cl	9.91	4.74	10.04	4.65	10.26	4.50	10.47	4.39
3-Cl	9.88	4.70	10.07	4.66	10.26	4.54	10.48	4.45
4-Cl	9.91	4.71	10.05	4.65	10.25	4.55	10.46	4.43
2-Br	9.91	4.64	10.03	4.58	10.26	4.48	10.44	4.41
3-Br	9.93	4.69	10.05	4.63	10.27	4.55	10.48	4.44
4-Br	9.89	4.69	10.05	4.62	10.25	4.54	10.50	4.46
2-NO_2	9.83	4.71	10.05	4.62	10.25	4.50	10.48	4.42
3-NO_2	9.86	4.70	10.04	4.63	10.25	4.55	10.49	4.48

R	50% *Et*OH (0.236)[a]		60% *Et*OH (0.316)[a]		70% *Et*OH (0.418)[a]		80% *Et*OH (0.552)[a]	
	$\log K_{OH}$	$\log K_{NH}$	$\log K_{OH}$	$\log K_{NH}$	$\log K_{OH}$	$\log K_{NH}$	$\log K_{OH}$	$\log K_{NH}$
H	10.64	4.36	10.70	4.25	10.76	4.18	10.80	4.15
2-CH_3	10.63	4.31	10.70	4.20	10.74	4.17	10.80	4.15
3-CH_3	10.64	4.28	10.71	4.20	10.75	4.17	10.79	4.15
4-CH_3	10.63	4.26	10.70	4.20	10.74	4.16	10.78	4.15
2-OCH_3	10.64	4.40	10.70	4.25	10.75	4.20	10.79	4.17
4-OCH_3	10.66	4.38	10.71	4.25	10.76	4.20	10.79	4.15
3-F	10.67	4.30	10.71	4.22	10.76	4.18	10.80	4.15
4-F	10.67	4.30	10.72	4.19	10.75	4.14	10.79	4.10
2-Cl	10.67	4.25	10.73	4.20	10.76	4.15	10.80	4.10
3-Cl	10.61	4.34	10.73	4.28	10.78	4.20	10.83	4.14
4-Cl	10.61	4.33	10.73	4.27	10.77	4.15	10.81	4.14
2-Br	10.60	4.29	10.74	4.20	10.76	4.18	10.81	4.14
3-Br	10.62	4.33	10.73	4.23	10.77	4.20	10.81	4.15
4-Br	10.59	4.35	10.71	4.25	10.75	4.16	10.80	4.15
2-NO_2	10.54	4.29	10.58	4.20	10.64	4.12	10.67	4.09
3-NO_2	10.56	4.35	10.61	4.20	10.74	4.13	10.80	4.06

[a] The mole fraction of ethanol

BA and *SA* can also be explained by comparing the conformational structures of these compounds. Spectroscopic studies show existence of strong intramolecular hydrogen bonding in *Schiff* bases such as salicylideneaniline (*SA*), but hydrogen bonding is not observed in the benzylideneanilines (*BA*) because of unfavorable steric conditions [31]. Thus, in the case of *SA*, the electron density of the hydrogen acceptor azomethine nitrogen atom decreases and the observation of lower logK_{NH} values for the *SA* derivatives can be explained in terms of stereochemistry. However, when it comes to logK_{OH}, in *SA*, where an intramolecular hydrogen bonded structure formed by the proton of the phenolate ion is more probable, one would have expected that the logK_{OH} values should have been higher than those of *BA*, contrary to experimental findings. This fact suggests that solute-solvent interactions as well as inductive effects are also important in the determination of the numerical values of the protonation constants of *Schiff* bases.

Moreover, the logK_{NH} values of the *Schiff* bases, a tertiary amine type derivative, and the primary amine 2-hydroxaniline [18] are approximately the same for each ethanol-water mixtures. The electron densities of the nitrogen atom in the case of *Schiff* bases is greater than in the case of 2-hydroxyaniline because of substituents with resonance and positive inductive effect (*i.e.*, an electron donating effect). However, the protonated form of the primary amine was stabilized by the greater number of water molecules involved in its hydration sphere [32] when compared with corresponding tertiary amine *Schiff* bases [33], thus the protonation constants of 2-hydroxyaniline should be greater than those of the *Schiff* bases studied. These findings were consistent with the reports in the literature for similar secondary and tertiary amines [34].

It is known that one of the most important factors determining the equilibrium constants is the reaction medium. The data given in Table 1 show that there is a nonlinear increase in the logK_{OH} values as well as a nonlinear decrease in the logK_{NH} values as the solvent becomes enriched in the organic component. In Figs. 2 and 3, the logK_{NH} and logK_{OH} values are plotted against the reciprocal of dielectric constant (ε^{-1}) of ethanol-water mixtures, showing a nonlinear variation of the log$K$ values with increasing *Et*OH concentrations.

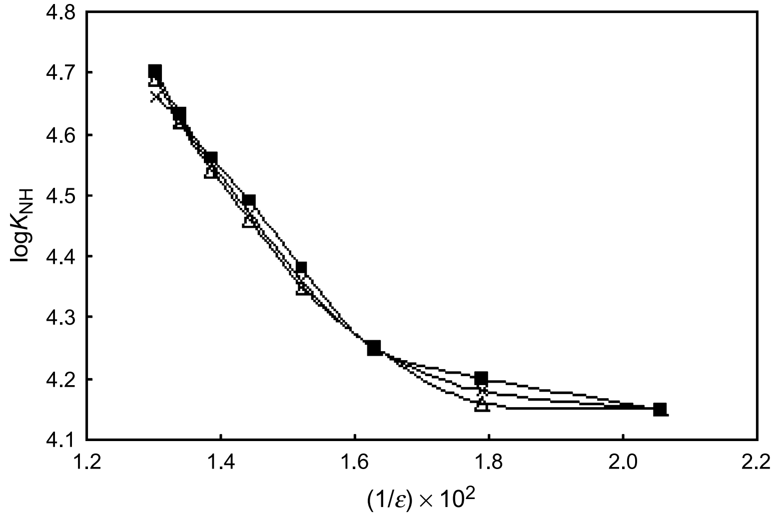


Fig. 2. The variation of logK_{NH} for some *Schiff* bases with the reciprocal of dielectric constants of ethanol-water mixtures (▲: *N*-benzylidene-2-hydroxyaniline; ■: *N*-(4-methoxybenzlidene)-2-hydroxyaniline; △: *N*-(4-bromobenzylidene)-2-hydroxyaniline)

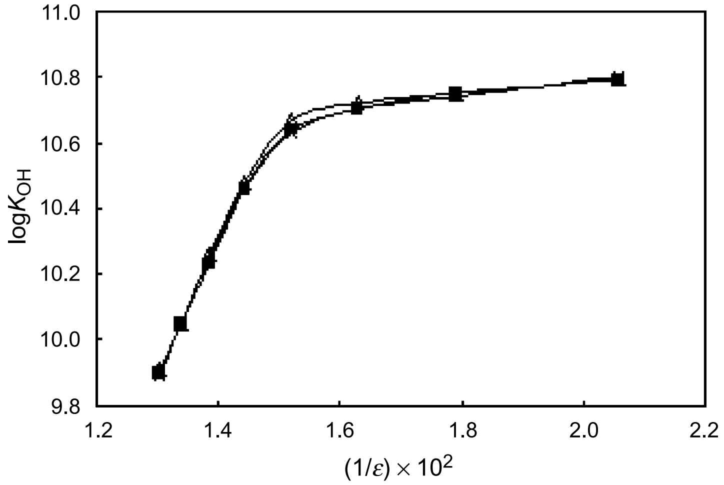


Fig. 3. The variation of $\log K_{OH}$ for some *Schiff* bases with the reciprocal of dielectric constants of ethanol-water mixtures (×: *N*-(2-methylbenzylidene)-2-hydroxyaniline; ■: *N*-(2-methoxybenzylidene)-2-hydroxyaniline; △: *N*-(4-fluorobenzylidene)-2-hydroxyaniline)

The first protonation equilibrium ($\log K_{OH}$) regarding protonation equilibrium of phenolate ions ($SB^- + H^+ = HSB$) has a $z = 0$ and therefore the electrostatic term contributes to increase the $\log K_{OH}$ value when the dielectric constant of the medium decreases by addition of an organic solvent of which the dielectric constant is lower than that of water. These results suggest that the influence of the composition of ethanol-water mixtures on the $\log K_{OH}$ values of *Schiff* bases is dependent on the electrostatic effects taken into account in *Born*'s theory. However, the expected linear variation with $1/\varepsilon$ was not observed, thus giving further confirmation of the limitations of the simple *Born* theory. Indeed, it has become clear that a purely electrostatic treatment is inadequate to account for solvent effects on the protonation constants of the neutral acids such as HA [35, 36]. The curvature of the experimental plot may be explained by non-electrostatic contributions to $\log K_{OH}$ values.

However, the second protonation equilibrium regarding protonation equilibrium of azomethine nitrogene ($\log K_{NH}$) has $z = 1$ and there is no change in the number of charges ($HSB + H^+ = H_2SB^+$), thus there is no electrostatic contribution to the $\log K_{NH}$ value of this equilibrium. Only the variations of the basicity of the solvent and of the specific solute-solvent interactions determine the variation of the $\log K_{NH}$ values of *Schiff* bases when the solvent composition is changed.

Consequently, it can be said that it is difficult to interpret the $\log K$ variations of the *Schiff* bases studied with only the macroscopic parameters of the ethanol-water mixtures. Therefore, in Fig. 4, the $\log K$ values of *Schiff* bases are plotted against the corresponding mixed solvent $E_T(30)$ values. It is clear that the correlation is much better than that obtained with only an electrostatic model. Thus, correlating $\log K$ values of *Schiff* bases with microscopic parameters is valid. It could be of interest to compare the microscopic parameters of ethanol-water mixtures with macroscopic ones present in bulk solution. Although, ε and $E_T(30)$ are both polarity parameters, a nonlinear ε^{-1} *vs.* $E_T(30)$ plot is obtained (Fig. 5), revealing that these

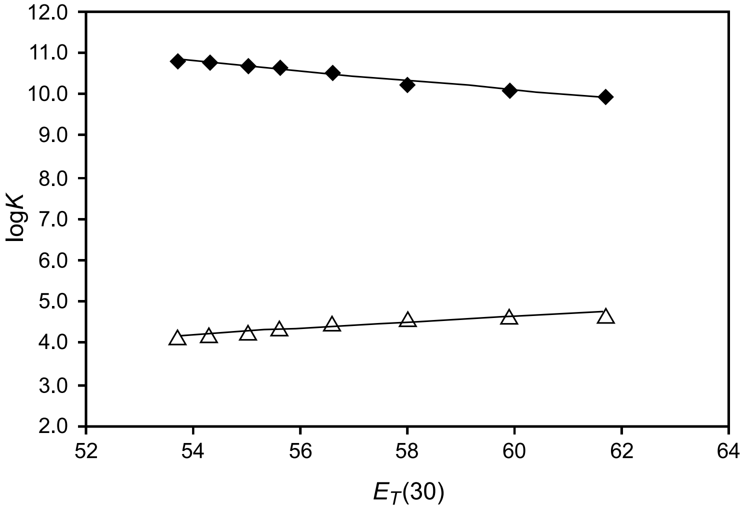


Fig. 4. The variation of $\log K_{OH}$ and $\log K_{NH}$ values for *N*-benzylidene-2-hydroxyaniline with $E_T(30)$ of ethanol-water mixtures (△: $\log K_{OH}$ values, ◆: $\log K_{NH}$ values)

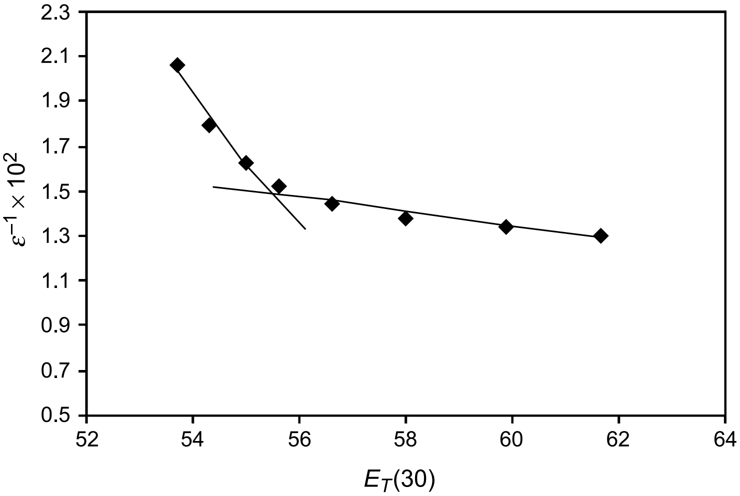


Fig. 5. The variation with ε^{-1} *vs.* $E_T(30)$ of ethanol-water mixtures

have different natures. It is not surprising, since dielectric constant, ε, represents the polarity in the bulk solution, whereas $E_T(30)$ describes the polarity of the solvation microsphere [1, 37]. The ε^{-1} *vs.* $E_T(30)$ plot shows that two linear portions are intersecting at $x_{EtOH} \cong 0.3$. The first portion is assigned to the water-rich zone ($x_{EtOH} \leq 0.3$, $\varepsilon^{-1} = -0.034E_T(30) + 3.367$, $r^2 = 0.964$, $F = 39.7$) and the second one to the ethanol-rich zone ($x_{EtOH} \geq 0.3$, $\varepsilon^{-1} = -0.327E_T(30) + 19.606$, $r^2 = 0.965$, $F = 27.8$). The different nature of the two polarity quantities $E_T(30)$ and ε^{-1} may be the reason why a purely electrostatic model is inadequate to account for solvent effects on the protonation constants of *Schiff* bases studied. The variation of the protonation constants of the *Schiff* bases studied with the percentage of ethanol could be explained by the fact that these protonation constants depend on the solute-solvent interaction effects and these effects change with the structural features of the mixture [38–40].

In the water-rich region of ethanol-water mixtures ($x_{EtOH} \leq 0.07$), the ethanol gradually occupies the cavities between water molecules without disrupting the water structure [38, 39]. In this water rich region, logK_{NH} values do not vary in contrast with logK_{OH} values because of the influence of changes in dielectric constant. In the range about $0.07 \leq x_{EtOH} \leq 0.45$, there are clusters of molecules of the same kind surrounded by a region where molecules of both kinds are near each other, which is called a microheterogeneity region. In this middle range of compositions the influence of ethanol is strongly disrupting the water structure and solute-solvent interactions can change. This might explain the variation in the log$K$ values of protonated azomethine nitrogen.

Although, the log$K$ values of the *Schiff* bases obtained in ethanol-water mixtures are smaller than expected considering the high log$K$ values expected in neat ethanol [18, 41]. The log$K$ values of the *Schiff* bases studied in neat ethanol are not known, but the log$K_{OH} = 15.8$ for phenol and log$K_{NH} = 5.60$ for aniline in neat ethanol were determined in earlier studies [41, 42]. The variation of the log$K$ values of the *Schiff* bases in ethanol-water mixtures could be preferential solvation in these media [38], which is a structural feature of these mixtures [14]. The deviation from the ideal dependence on the composition of the mixture indicates that the solvent composition in the neighborhood of the solute may be different from that in the bulk. In our previous works [18, 19], the QLQC theory of preferential solvation [38] was applied to find the point of preferential solvation of hydrogen ions in ethanol-water mixtures. The deviation from ideal dependence on the composition of the mixture to lower log$K$ values indicates a preferential solvation by water as previously examined in these studies [18, 19]. Therefore, the log$K$ values of substances in these mixtures are more similar to log$K$ values in water than those in ethanol.

These investigations also provide significant evidence that FA techniques can contribute to better understanding of solute-solvent interactions in these mixtures. *Taft et al.* proposed the use of solvatochromic parameters in order to evaluate solute-solvent interactions for many *Gibbs* free energy-related properties, including protonation of bases in water and organic-water solvent mixtures [25, 43], through correlation analysis, Linear Solvation Energy Relationships (LSER). For this purpose, in this study, two data matrices were constructed from the logK_{OH} and logK_{NH} values that correspond to the protonation reactions of the functional groups of the *Schiff* bases studied.

Factor analysis applied to the matrices show that the number factors responsible for variations of logK_{OH} and logK_{NH} values of *Schiff* bases studied when solvent composition changes is three for two data matrices. Target factor analysis applied to log$K$ values gives the following results: the targets, which fit better the log$K$ data, are unity, α, and π^* parameters for the hydrogen bond donating ability and dipolarity/polarizability, respectively. Other combinations of factors were tried to explain mixed solvent-solute interactions, but the fit of the model proposed to reproduce experimental data was worse. In Tables 2 and 3, *Kamlet-Taft* equations arising from the application of FA and TFA to the analyzed matrices are shown. Global errors in data reproduction (*RMS* and *RSD*) were in agreement with experimental errors.

Table 2. Expressions of *Kamlet-Taft* equations obtained through factor analysis and target factor analysis applied to data built from $\log K_{\mathrm{OH}}$ values of *Schiff* bases; *RMS* (root-mean-square error) = 0.08; *RSD* (residual standard deviation) = 0.06; error associated to values are given in parenthesis

Schiff bases	Linear solvation energy relationships (LSER)
N-benzylidene-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.579(0.09) + 0.338(0.13)\pi^* + 2.794(0.19)\alpha$
N-(2-methylbenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.627(0.07) + 0.289(0.10)\pi^* + 2.905(0.15)\alpha$
N-(3-methylbenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.574(0.09) + 0.328(0.12)\pi^* + 2.808(0.18)\alpha$
N-(4-methylbenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.600(0.08) + 0.284(0.13)\pi^* + 2.889(0.15)\alpha$
N-(2-methoxybenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.619(0.08) + 0.314(0.11)\pi^* + 2.872(0.16)\alpha$
N-(4-methoxybenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.519(0.09) + 0.308(0.12)\pi^* + 2.714(0.20)\alpha$
N-(3-fluorobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.678(0.10) + 0.317(0.11)\pi^* + 2.867(0.18)\alpha$
N-(4-fluorobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.619(0.08) + 0.298(0.12)\pi^* + 2.899(0.17)\alpha$
N-(2-chlorobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.571(0.07) + 0.319(0.13)\pi^* + 2.814(0.19)\alpha$
N-(3-chlorobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.602(0.09) + 0.301(0.11)\pi^* + 2.798(0.16)\alpha$
N-(4-chlorobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.628(0.05) + 0.410(0.07)\pi^* + 2.771(0.10)\alpha$
N-(2-bromobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.628(0.10) + 0.433(0.14)\pi^* + 2.752(0.20)\alpha$
N-(3-bromobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.602(0.07) + 0.352(0.15)\pi^* + 2.796(0.15)\alpha$
N-(4-bromobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.637(0.07) + 0.271(0.10)\pi^* + 2.931(0.15)\alpha$
N-(2-nitrobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.210(0.12) + 0.234(0.14)\pi^* + 2.513(0.19)\alpha$
N-(3-nitrobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{OH}} = 13.310(0.11) + 0.338(0.13)\pi^* + 2.600(0.18)\alpha$

Table 3. Expressions of *Kamlet-Taft* equations obtained through factor analysis and target factor analysis applied to data built from $\log K_{\mathrm{NH}}$ values of *Schiff* bases; *RMS* (root-mean-square error) = 0.07; *RSD* (residual standard deviation) = 0.05; error associated to values are given in parenthesis

Schiff bases	Linear solvation energy relationships (LSER)
N-benzylidene-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.808(0.08) + 0.859(0.12)\pi^* + 0.718(0.18)\alpha$
N-(2-methylbenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.592(0.11) + 0.627(0.16)\pi^* + 1.158(0.23)\alpha$
N-(3-methylbenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.539(0.06) + 0.447(0.08)\pi^* + 1.383(0.12)\alpha$
N-(4-methylbenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.432(0.05) + 0.275(0.07)\pi^* + 1.661(0.10)\alpha$
N-(2-methoxybenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.799(0.13) + 0.788(0.19)\pi^* + 0.818(0.27)\alpha$
N-(4-methoxybenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.749(0.10) + 0.848(0.15)\pi^* + 0.804(0.21)\alpha$
N-(3-fluorobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.575(0.07) + 0.527(0.10)\pi^* + 1.279(0.14)\alpha$
N-(4-fluorobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.445(0.11) + 0.700(0.15)\pi^* + 1.218(0.22)\alpha$
N-(2-chlorobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.214(0.07) + 0.403(0.11)\pi^* + 1.753(0.16)\alpha$
N-(3-chlorobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.662(0.07) + 0.713(0.11)\pi^* + 1.024(0.16)\alpha$
N-(4-chlorobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.548(0.08) + 0.698(0.12)\pi^* + 1.144(0.17)\alpha$
N-(2-bromobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.732(0.09) + 0.627(0.08)\pi^* + 1.100(0.11)\alpha$
N-(3-bromobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.642(0.06) + 0.453(0.13)\pi^* + 1.177(0.19)\alpha$
N-(4-bromobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.683(0.10) + 0.755(0.14)\pi^* + 0.948(0.20)\alpha$
N-(2-nitrobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.375(0.10) + 0.659(0.14)\pi^* + 1.323(0.20)\alpha$
N-(3-nitrobenzylidene)-2-hydroxyaniline	$\log K_{\mathrm{NH}} = 2.510(0.13) + 1.107(0.18)\pi^* + 0.744(0.26)\alpha$

For the protonation reactions corresponding to the unprotonated phenolate groups of *Schiff* bases, $\log K_{\mathrm{OH}}$, the coefficients of target α in the reduced *Kamlet-Taft* equations summarized for values in Table 2 are negative in all instances, which means that an increase on the solvation of the unprotonated phenolic oxygen by a hydrogen bond donor from the solvent to the *Schiff* bases is caused by an increase in the hydrogen bond donor capability of the solvent and therefore it decreases electrolyte ($SB^- + H^+ = HSB$) protonation and $\log K_{OH}$. Also, the factor loading for π^* obtained by TFA indicates the degree of significance of solute-solvent dipolarity/polarizability interaction. The coefficients of target π^* in Table 2 reveals that the protonation constant of solute increases by decreasing of π^* of the solvent and, hence, the basicity strength increases. There exists a dipole-dipole interaction between the polar *Schiff* bases and the polar solvent while an ion-dipole interaction is the important force between the polar solvent and unprotonated *Schiff* bases. Since the solute ion-solvent dipole interaction is stronger than the dipole-dipole interaction, increasing the polarity of the solvent causes the unprotonated form of *Schiff* bases to become more stable than protonated *Schiff* bases, thus the degree of protonation decreases. In recent QSPR study of the acidity constants of anthraquinones, it was found that the dipole moment of the unionized anthraquionones affects their acidity [44]. Furthermore, the coefficients of the α terms are higher than those of π^* terms indicating that the dependence of the protonation process on the H-bond-donating acidity of the solvent predominoles the whole range of composition studied.

An analysis of the various contributions to $\log K_{NH}$ corresponding to azomethine nitrogen shows (Table 3) that the coefficients of target π^* and α are always positive, which means that an increase in the polarity and the H-bond-donating acidity of the mixed solvent causes the $\log K_{NH}$ values to increase. Also, both effects have the same sign and can be added, thus increasing the total effect upon the $\log K_{NH}$ values.

This study confirms the usefulness of microscopic parameters, such as π^* and α in the explanation of microscopic processes since the solvent properties in the cybotactic zone are the ones which directly affect the solutes. Preferential solvation by water occurs in ethanol-water mixtures, in the range of compositions studied here, for hydrogen ions. Furthermore, the FA and TFA chemometric techniques enable us to obtain equations that permit calculation of $\log K$ values in these binary solvent mixtures up to 80% (v/v) of organic solvent and in pure water.

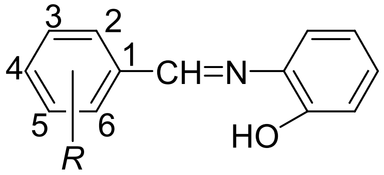
Experimental

Reagents

Schiff bases were prepared by the well-known amine-aldehyde condensation (2-hydroxyaniline with benzaldehyde and some substituted benzaldehydes) in ethanolic medium [45]. The *Schiff* bases obtained were purified by recrystallisation from ethanol. The *Schiff* bases are dark yellow crystalline solids. The solubility of the *Schiff* bases was examined in common solvents. They were insoluble in water, but were readily soluble in acetonitrile, formamide, methanol, ethanol, chloroform, 1,4-dioxane, *N*,*N*-dimethylformamide, and dimethylsulfoxide. The melting points agreed with those in the literature. The purity of these compounds was confirmed by a non-aqueous titrimetric method. The resulting *Schiff* bases have the following general structure (Scheme 2).

The derivatives used were $R = H$, 2-CH_3, 3-CH_3, 4-CH_3, 2-OCH_3, 4-OCH_3, 3-F, 4-F, 2-Cl, 3-Cl, 4-Cl, 2-Br, 3-Br, 4-Br, 2-NO_2, and 3-NO_2 benzylidene-2-hydroxyanilines. Approximately 0.03 *M* *Schiff* bases stock solutions were prepared in ethanol.

2-Hydroxyaniline and all substituted benzaldehydes were purchased from Merck and were used as received. All stock solutions of perchloric acid, sodium perchlorate, and potassium hydrogenphthalate



Scheme 2

(analytical reagent grade, all from Merck) were prepared by water (double-distilled and freshly boiled, whose conductivity did not exceed 0.05 μS cm^{-1}). Carbonate-free sodium hydroxide solutions (0.1 *M*) were prepared under a nitrogen atmosphere as 10, 20, 30, 40, 50, 60, 70 and 80% (v/v) aqueous ethanol solutions.

Procedure

Values of the emf of the potentiometric cell were measured with an Orion 960 automatic titrator equipped with Orion EA 940 *pH* meter (resolution 0.1 mV, accuracy 0.2 mm^3) using a Mettler Toledo Inlab 412 combined glass electrode under N_2 and at 25.0 ± 0.1°C. The electrode was modified by substituting its aqueous KCl solution for the mixture 0.01 *M* NaCl + 0.09 *M* $NaClO_4$. Apparatus is described in detail elsewhere [18].

The free hydrogen ion concentration, [H$^+$], in this cell was determined by measuring the emf of cell (Eq. (1)) in the course of the titrations.

$$E(\mathrm{mV}) = E^{\mathrm{o}}_{\mathrm{cell}} + s\log[\mathrm{H}^+] + E_j \tag{1}$$

where $s = \mathrm{R}T\ \log\frac{1}{\mathrm{F}}$

The standard potential in this cell, $E^{\mathrm{o}}_{\mathrm{cell}}$, was evaluated by means of series of emf measurements of $HClO_4$ solutions and the method of *Gran* from titrations of diluted $HClO_4$ solutions in the desired solvent using NaOH solutions in the same solvent as the titrant, and evaluation of the calibration parameters using multiparametric data fitting or *Gran* plots [46]. As liquid junction potential values, E_j, depend only on the ionic strength, they can be considered as constant in potentiometric titrations. Also, by assuming $E^{\mathrm{o}}_{\mathrm{cell}}$ value determined in the acidic range to be reliable and [OH$^-$] concentration was set by base added in excess, we calculated reproducible values of the stoichiometric ion products ($K_\mathrm{w} = [\mathrm{H}^+][\mathrm{OH}^-]$) of water for all the solvent mixtures at ionic strength of 0.10 *M* with $NaClO_4$ in several series of experiments.

Titrations were performed with carbonate-free standard 0.1 *M* NaOH on 50 cm^3 solution containing 0.1 *M* $NaClO_4$ and (i) 2.5×10^{-3} *M* $HClO_4$ (for cell calibration) plus (ii) 2.5×10^{-3} *M* $HClO_4$ + 1.5×10^{-3} *M Schiff* bases. During titrations, a potential reading was taken after waiting a suitable time for establishing the equilibrium after each addition of titrant.

Data Treatment

The stoichiometric protonation constants of the *Schiff* bases were computed from titration data using the FORTAN program BEST [47]. The number of experimental points (*v*, *pH*) was more than 38 (maximum 58) for each titration. In refining the overall constants, some experimental points, especially around the equivalent points, were neglected. The error in the constants listed in Table 1 is estimated as 0.02 log unit on the basis of the σ_{fit} value, which measures the deviation of the experimental curve and the curve calculated from the equilibrium constants, being less than 0.01 *pH* unit in all potentiometric determinations. The equilibrium constants reported in this paper were obtained as averaged values of four titrations.

The principle and methodologies of FA and TFA are described in detail by *Malinowski* [48]. In brief, an experimental data matrix (D) can be expressed by Eq. (2) where S and L respectively, are, the score and loading matrices of D for the preselected number of components; E is the residual error matrix containing the variance not explained by S and L, and D* is the reproduced data matrix based on S and L. The number of components to be considered is the number needed to reproduce the original data matrix within the experimental error.

$$D = SL + E = D^* + E \tag{2}$$

The data treatment was the same as that used in previous studies [18, 19]. Factor analysis was used first, to determine how many sources of independent variation (factors) were involved in the variation data. Afterwards, target factor analysis was applied to identify the chemical nature of these factors. The TFA enables us to test individually the suspected parameters, the target vectors (*i.e.*, physical properties) as possible real factors that may be responsible for trends in the data matrix. This individual testing ability is one of the most valuable features of TFA.

All calculations were performed through the Holmes 2000 program [49–51]. Also, MATLAB functions [52] were used to check the number of factors through singular value decomposition [53].

Finally, the definitive model for the original data matrix comes from the combinations of the accepted target vectors which best reproduce the original data matrix, yielding the lowest root-mean-square (*RMS*) error. The set of selected target vectors is arranged in a key combination matrix which, when multiplied by the factor loading matrix, gives the reproduced data matrix. Therefore, the user – guided by theoretical considerations or chemical intuition – may select from among the target combinations in order to attain the optimum set. Also, the residual standard deviation value (*RSD*) was calculated since it gives a more realistic precision in the fit.

Values of the *Kamlet-Taft* solvatochromic parameters (α, π^*, β [54, 55], and $E_T(30)$ (or E_T^N) [56]) were taken from the literature.

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