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Determination of Acidity Constants of 4-(2-Pyridylazo)resorcinol in Binary Acetonitrile + Water Mixtures

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The acid−base properties of 4-(2-pyridylazo)resorcinol in binary mixtures of acetonitrile + water are studied by a multiwavelength spectrophotometric method. To evaluate the pH−absorbance data, a resolution method based on the combination of soft- and hard-modeling is applied. The acidity constants of all related equilibria are estimated using the whole spectral fitting of the collected data to an established factor analysis model. The corresponding pK_a values have been determined in all binary mixtures of acetonitrile + water. There is a linear relationship between acidity constants and the mole fraction of acetonitrile in the solvent mixtures. The effect of solvent properties on acid−base behavior is discussed.

1. Introduction

Acid dissociation constants are important parameters to indicate the extent of ionization of molecules in solution at different pH values. The acidity constants of organic reagents play a fundamental role in many analytical procedures such as acid−base titration, solvent extraction, complex formation, and ion transport. It has been shown that the acid−base properties affect the toxicity,[1] chromatographic retention behavior, and pharmaceutical properties[2] of organic acids and bases. Much of the theoretical foundation of modern organic chemistry is based on the observation of the effects on acid−base equilibrium of changing molecular structure.[3]

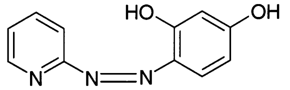
Acetonitrile is one of the most important dipolar aprotic solvents, it is used extensively as a reaction medium for mechanistic studies, in electrochemistry, and in high performance liquid chromatography and it is also employed as a solvent for nonaqueous titrations.[4] Acetonitrile behaves as a weaker base and as a much weaker acid than water. It has a relatively high dielectric constant ($\epsilon = 36$) and a small autoprotolysis constant (p$K_s = 33.6$). Accordingly, acetonitrile acts as a strongly differentiating solvent with a modest solvating power for many polar ionic solutes.[5,6] Poorly water soluble drugs require a water miscible cosolvent to solubilize them. When the pK value of a drug in water is required but is not available due to its water insolubility, an indirect estimation from its ionization constant evaluated in a suitable solvent mixture could solve the problem.[7]

The spectroscopic instrumentation used today, however, almost invariably has the capacity to collect data in a full spectral range. Using a single or a few wavelengths discards most of the information in the collected spectra and requires both the presence of and knowledge of such suitable wavelengths. However, in many cases, the spectral responses of components overlap and analysis is no longer straightforward.[8,9]

The predefined model, known as hard-modeling analysis, cannot be applied if crucial information is missing. Soft-modeling or model free approaches are based on much more general prerequisites, such as positive molar absorbance, positive concentration of all species, unimodality of concentration profiles, and closure (concentration of all species are the same for all solutions). Naturally, if the strengths of hard-modeling and soft-modeling methodologies are combined, a much more powerful method of data analysis can be expected.[10−12] The principle component analysis along with different curve resolution methods[13−23] have been applied to spectral data to extract information utilizing a large number of absorbances measured at different wavelengths.

2. Theory

The spectra of 4-(2-pyridylazo)resorcinol [CAS RN 1141-59-9] (PAR, **I**) at different pH values are digitized and arranged in a data matrix **X** with size of *ns* × *nw*, where *ns* denotes the number of spectra and *nw* the number of wavelengths for which absorbances were recorded. Under the assumption of bilinearity, **X** can be described by the concentration profiles ($\mathbf{c}_i$, $ns \times 1$) and the pure analyte spectra ($\mathbf{a}_i$, $1 \times nw$) according to



I

$$\mathbf{X} = \sum_{i=1}^{nc} c_i a_i = \mathbf{CA} + \mathbf{E}_1 \tag{1}$$

where *nc* is the number of chemical components. $\mathbf{E}_1$ is the residual matrix and should contain only noise. PCA decomposes the spectral data matrix into a score **T** and a loading matrix **P** ($\mathbf{P}^T$ is the transpose of **P**):

$$\mathbf{X} = \mathbf{TP}^T + \mathbf{E}_2 \tag{2}$$

With the correct number of principal components, that is, equal to *nc*,[24−26] $\mathbf{E}_2$ is a residual matrix and contains insignificant information. Concentration profiles and pure component spectra are a linear combination of the **T** and

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P matrixes; thus,

$$\mathbf{C} = \mathbf{T}\mathbf{R}^{-1} \tag{3}$$

$$\mathbf{A} = \mathbf{R}\mathbf{P}^{\mathrm{T}} \tag{4}$$

in which **R** ($nc \times nc$) is a square transformation matrix. From a known (or tested) system of equilibrium equations describing the system and the trial values of equilibrium constants, concentration profiles $\mathbf{c}_{\mathrm{sim},i}$ ($ns \times 1$) for all species at each pH value can be calculated. The concentration vectors for all species are gathered in a matrix $\mathbf{C}_{\mathrm{sim}}$, and a least-squares fit is performed (cf. eq 3):

$$\mathbf{R}^{-1} = (\mathbf{T}^{\mathrm{T}}\mathbf{T})^{-1}\mathbf{T}^{\mathrm{T}}\mathbf{C}_{\mathrm{sim}} \tag{5}$$

Target testing has been applied to a variety of problems and proved to be a useful technique.[27−32] So, according to a standard target testing procedure,[27] if eq 5 is inserted in eq 3, we obtain a matrix $\mathbf{C}_{\mathrm{calc}}$ and then the residual matrixes $\mathbf{C}_{\mathrm{res}}$ and $\mathbf{T}_{\mathrm{res}}$, calculated as

$$\mathbf{C}_{\mathrm{res}} = \mathbf{C}_{\mathrm{sim}} - \mathbf{C}_{\mathrm{calc}} = \mathbf{C}_{\mathrm{sim}} - \mathbf{T}\mathbf{R}^{-1}\ (= \mathbf{C}_{\mathrm{sim}} - \mathbf{T}(\mathbf{T}^{\mathrm{T}}\mathbf{T})^{-1}\mathbf{T}^{\mathrm{T}}\mathbf{C}_{\mathrm{sim}}) \tag{6}$$

$$\mathbf{T}_{\mathrm{res}} = \mathbf{T} - \mathbf{T}_{\mathrm{calc}} = \mathbf{T} - \mathbf{C}_{\mathrm{sim}}\mathbf{R} \tag{7}$$

The $\mathbf{C}_{\mathrm{res}}$ and $\mathbf{T}_{\mathrm{res}}$ can be used in different ways in an objective function that has a minimum for $\mathbf{C}_{\mathrm{sim}} = \mathbf{C}$, that is, for a $\mathbf{C}_{\mathrm{sim}}$ calculated using the correct equilibrium constant. A computer program based upon the Levenberg−Marquardt algorithm[33] was written in MATLAB (Mathworks, version 6.1) and used to refine the acidity constants.

3. Experimental Section

The pure reagent PAR, acetic acid, boric acid, phosphoric acid, sodium hydroxide, and potassium nitrate were all from Merck Company, and Fluka extra pure acetonitrile was used. The absorption spectra were recorded using a CECIL 9050 spectrophotometer. The pH measurements were made using a Metrohm 692 pH meter equipped with a glass calomel combined electrode. To calibrate the pH meter in the various binary acetonitrile + water mixtures used, 0.01 M solutions of oxalate and succinate buffers were employed. The reference values of the pH, according to the activity scale, of these buffer solutions in different acetonitrile + water mixtures have been reported previously.[34−36] In all experiments, the ionic strengths of the solutions used were kept constant at 0.1 M using potassium nitrate as the supporting electrolyte. A stock solution (2.0×10^{-5} M) of PAR was prepared. The pH values in acetonitrile + water solvent mixtures were corrected using the equation $\mathrm{pH}^* = \mathrm{pH(R)} - \delta$, where pH* is the corrected reading and pH(R) is the pH-meter reading obtained in a partially aqueous organic solvent, determined by Douheret.[35,36] All measurements were carried out at the temperature (25 ± 0.5) °C.

4. Results and Discussion

The electronic absorption spectra of PAR in binary solvent mixtures at various pH values at 380−580 nm intervals were recorded. Sample spectra of PAR at different pH values in pure water and 80 vol % acetonitrile to water are shown in Figures 1 and 2, respectively. The principal component analysis of all absorption data matrices obtained at various pH values shows at least four significant factors that also supported by the statistical indicators of Elbergali et al.[37] These factors could be attributed to the three dissociation equilibria of a triprotic acid such as PAR. The pK_a values of PAR were investigated in nine different acetonitrile + water binary mixtures spectrophotometrically at 25 °C. Acidity constants of PAR in several mixtures were evaluated using the above algorithm using the corresponding spectral absorption−pH data. From inspection of the experimental spectra, it is hard to guess even the number of protolytic species involved. The four calculated most significant projection vectors with clear spectral features (as compared to noise) evidence the presence of four spectroscopically distinguishable components. Their shapes, however, are clearly unphysical and cannot be directly related to the spectral response of the four protolytic forms. The output of the program is pK_a values and their standard deviation, the number of principal components, projection vectors (loadings), concentration distribution diagrams, and the pure spectrum of each assumed species. The obtained pK_a values are listed in Table 1. The pK_a values correspond to the pH dependent variation of absorption spectra in all solvent mixtures. The previous reported values of acidity constants are mainly in mixtures of dioxin, methanol, and ethanol with water. The obtained values in pure water are in good agreement with previous values,[38,39] which are listed in Table 1 for comparison. The differences observed between the pK_a values of the second and third steps are due to probable experimental errors of

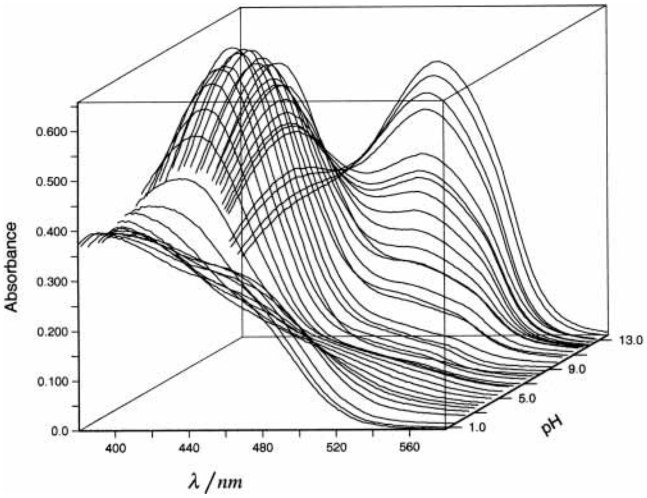

Figure 1. Absorption spectra of PAR in pure water at different pH values.

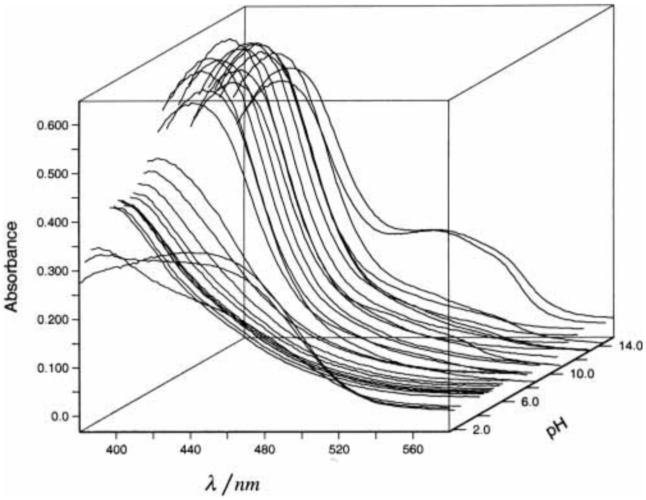

Figure 2. Absorption spectra of PAR in 80 vol % acetonitrile to water at different pH values.

Table 1. Acidity Constants of PAR at Different Mole Fractions of Acetonitrile (x_1) at 25 °C and Constant Ionic Strength (0.1 M KNO_3)

	acidity constants		
x_1	pK_{a1}	pK_{a2}	pK_{a3}
0	3.09 ± 0.02	5.46 ± 0.02	12.3 ± 0.1
	3.03[a]	5.57[a]	11.95[a]
	3.02[b]	5.56[b]	11.98[b]
0.046	2.75 ± 0.04	15.61 ± 0.04	12.2 ± 0.1
0.099	2.78 ± 0.04	5.94 ± 0.04	13.1 ± 0.1
0.158	2.47 ± 0.02	6.27 ± 0.06	13.0 ± 0.1
0.226	2.42 ± 0.01	6.48 ± 0.05	13.0 ± 0.2
0.304	2.41 ± 0.01	6.67 ± 0.06	13.2 ± 0.2
0.396	2.43 ± 0.05	6.94 ± 0.05	14.5 ± 0.2
0.505	2.28 ± 0.06	7.12 ± 0.05	14.7 ± 0.2
0.636	2.33 ± 0.07	7.52 ± 0.05	14.6 ± 0.5

[a] Reference 38. [b] Reference 39.

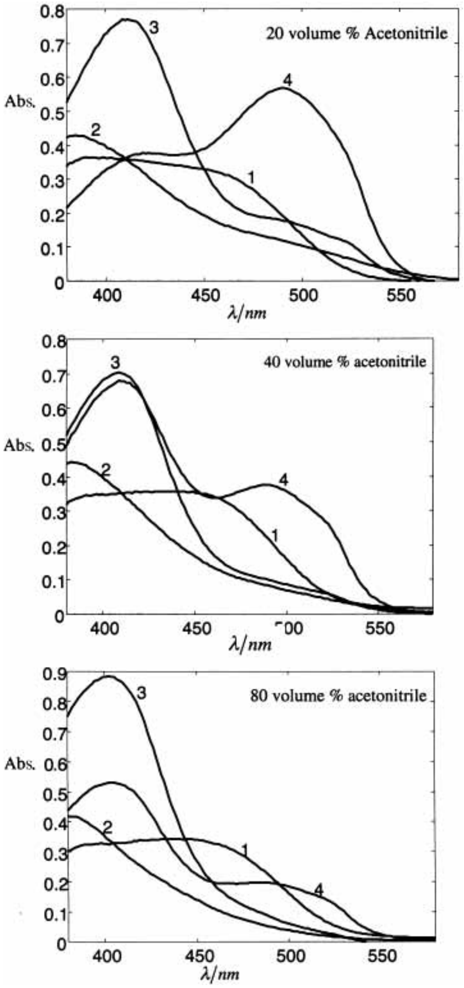

Figure 3. Pure spectra of PAR species in the various mixtures of acetonitrile + water: H_3L^+ (1), H_2L (2), HL^- (3), L^{2-} (4).

old methods, since chemometrics based methods, by using the whole spectral domain, reduce considerably the level of noise. So the obtained acidity constants are more reliable and precise than previous methods. One of the very important outputs of the algorithm is the calculated spectrum of different forms of PAR in each solvent mixture. The calculated spectra of all species in different solvent mixtures are shown in Figure 3. It is interesting to note that the nature of the solvent composition has a fundamental effect on each pure spectrum. As is clear from Figure 3, this effect is more for H_3L^+ and L^{2-} than for H_2L and HL^-. The spectrum of the L^{2-} species has a λ_{max} at 490 nm and a shoulder at about 410 nm. The solvent effect on this spectrum is very interesting. As the mass factor of acetonitrile increased, the absorption intensity at 490 nm decreased and that at 410 nm increased. This can be described using the nonelectrostatic (H-bonding) property of the stabilization and/or destabilization of the ground and excited states of the n → π* and π → π* transitions. The most important features of the distribution diagrams are the pH limits of the evolving and disappearing of components. The distribution diagrams are shown in Figure 4.

The pK_a values of PAR obtained in acetonitrile−water mixtures increase with percentage of acetonitrile. These variations could be explained by the fact that there is preferential solvation in these media that is related to the structural features of these mixtures. Preferential solvation in acetonitrile−water mixtures produces lower pK_a values than those expected when the preferred solvent is water. The composition of the immediate surroundings of a solute may differ from the composition of the bulk mixture. Preferential solvation is attributable to an excess or deficiency of molecules of one of the solvents in these surroundings.[40] If the solute displays no preference for the solvent molecules, the solvent composition in the primary coordination shell, in the immediate neighborhood of the solute, is the same as that in the bulk. The deviation from the ideal dependence on the composition of the mixtures indicates that the solvent composition in the neighborhood of the solute may be different from that in the bulk.

As discussed above, the data shown in Table 1 clearly illustrate the important influence of the nature of the solvent on the dissociation reaction. It has been shown that the solvating ability[41] (as expressed by the Guttmann donicity scale) and dielectric constant of the solvent play a fundamental role in dissociation reactions. Water is a solvent of high solvating ability (i.e. donor number DN = 33.0 and dielectric constant $\epsilon = 78$) which can dissociate the acid and stabilize the produced anion and hydrogen ion. Thus, it is expected that addition of acetonitrile with lower donor number and dielectric constant (DN = 14.0, $\epsilon = 36.0$) to water decreases the extent of interaction of the acid anion and the proton with solvent, and this decreases the acidity constant of the acid. It is interesting to note that there is actually a linear relationship between the pK_a values of the three dissociation steps (that of the first step decreases, and those of the second and third steps increase) and the mole fraction of acetonitrile ($x_{acetonitrile}$) in the binary mixed solvents that are shown in Figure 5. The same trend has already been reported for various organic molecules in different solvent mixtures.[12,42,43] It has been reasonably assumed that preferential solvation of the charged particles by water is mainly responsible for such a monotonic dependence of the acidity constants of PAR on the solvent composition. It is clear that the dissociation of an uncharged acid in a solvent requires the separation of two ions of opposite charges. The work required to separate these charges is inversely proportional to the dielectric constant of the solvent. The energy required for dissociation is supplied by solvation of the ions, and also the proton transfer from acid to the solvent molecule supplies an additional energy. If the dielectric constant and the solvating ability of the solvent are decreased, more energy will be required to separate the anion and cation, and consequently the extent of dissociation of the acid will be lowered. Therefore, the increase in the pK_a of the first step and the decrease in those of the second and third steps are due to increasing the mole fraction of acetonitrile in the binary mixed solvent.

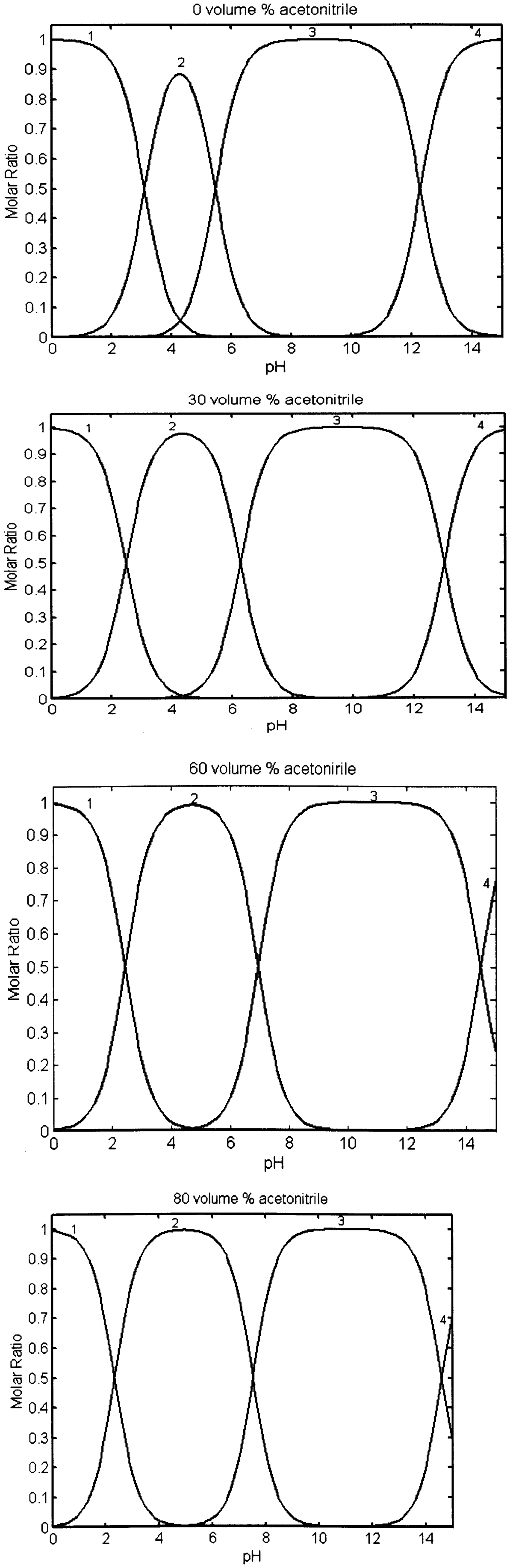

Figure 4. Distribution diagram of different species of PAR in water + acetonitrile mixtures: H_3L^+ (1), H_2L (2), HL^- (3), L^{2-} (4).

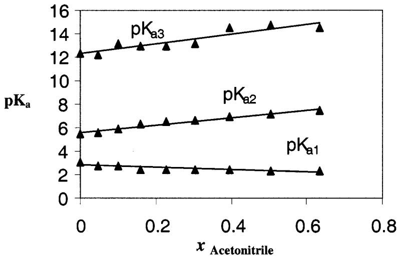

Figure 5. Plot of pK_a values against mole fraction of acetonitrile in the binary mixed solvents water + acetonitrile.

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