Spectrophotometric determination of acidity constants of 4-(2-pyridylazo)resorcinol in binary methanol–water mixtures

J. Ghasemi [a,*], A. Niazi [a], M. Kubista [b], A. Elbergali [b]

[a] *Department of Chemistry, Razi University, Kermanshah, Iran*
[b] *Department of Molecular Biotechnology, Chalmers University of Technology, Goteborg, Sweden*

Abstract

The acidity constants of 4-(2-pyridylazo)resorcinol (PAR, Scheme 1) in binary mixtures of methanol–water at 25 °C and an ionic strength of 0.1 M have been determined spectrophotometrically. DATa ANalysis (DATAN) program applied for determination of acidity constants. As percent of methanol increases in solvent mixtures the pK_a constants also increased. There is linear relationship between acidity constants and the mole fraction of methanol in the solvent mixtures. Effect of solvent composition on acidity constants and pure spectrum of each component are also discussed. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: 4-(2-Pyridylazo)resorcinol; Principal components; DATAN; Acidity constants; Binary solvents; Solvent mixtures

1. Introduction

The accurate determination of acidity constant values is often required in various chemical and biochemical areas. These are of vital importance in understanding the distribution, transport behavior, binding to receptors and mechanism of action of certain pharmaceutical preparation [1,2]. The acidity constants of organic reagents play a very fundamental role in many analytical procedures such as acid–base titration, solvent extraction and complex formation. But in determining of acidity constants of these molecules we are faced with several drawbacks, such as low solubility in aqueous solutions and the low values of acidity constants. Therefore, in order to enhance the acidity

constants on one hand and to increase the solubility on the other, we forced to choose mixed solvents.

Mixed solvents are interesting, because two solvents mixed together produce a solvent with quite different properties, both, physically (dielectric, density and viscosity) and chemically (acid–base and donor–acceptor properties). As far as the acid–base properties are concerned, an important feature is that the nature of the solvent is crucial for the strength of acids and bases. In particular, important is the proton affinity, in other words, the proton-donating and proton-accepting properties of solvent, as well as its polarity. In addition, the ionization degree of solute depends on the dielectric constant of solvent. Media of high dielectric constants are strongly ionizing, whereas those of low dielectric constants ionize to a lesser extent [3]. By mixing solvents of different polarity in proper ratios, dielectric constant of the medium can be varied and, at the same time, the strength of dissolved acids and bases [4]. It should

---

* Corresponding author. Tel.: +98-831723306;
fax: +98-8318231618.
E-mail address: ghasemij@yahoo.com (J. Ghasemi).
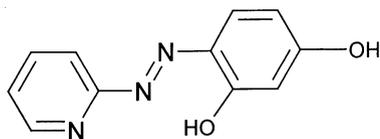
Scheme 1.

also be emphasized that solvent mixtures can be more convenient than individual solvents owing to enhanced solubilising efficiency, increased sharpness of color change of indicators during titration and more manageable shape of acid–base titration curves [5,6].

Spectroscopic methods are, in general, highly sensitive and are as such suitable for studying chemical equilibria solution. If the components involved can be obtained in pure form, or if their spectral responses do not overlap, such analysis is, in general, trivial. For many systems, particularly those with similar components, this is not the case, and these have been difficult to analyze. Therefore, to overcome this problem we have to employ the graphical and computational methods. Up to the middle of the 1960s, the evaluation of equilibrium measurements was based on the different graphical methods. These methods were reviewed in considerable details by Rossotti and Rossotti [7]. Starting from middle of the 1960s, computers acquired ever-greater importance in the evaluation of equilibrium measurement data using multiple wavelengths or full spectrum to determining the stability and acidity constants. The most relevant reports are on LETAGROP-SPEFO [8], SPECFIT [9], SQUAD [10] and HYPERQUAD [11]. All these computational approaches are based on an initial proposal of a chemical equilibrium model defining species stoichiometries and based on mass-action law and mass balance equations (hard modeling methods) and also involve least-squares curve-fitting procedures.

The starting point of using soft modeling was in 1971 that Lawton and Sylvestre [12] introduced chemometrics-based method for spectral analysis. These approaches are free from the restriction of the mass-action law and do not require an initial model of species to be set up. Recently, Kubista et al. [13,14] developed a new method, called the physical constraints approach, which provides a unique solution by requiring that the calculated concentrations obey an assumed equilibrium expression and demonstrates

its applicability by determining the acidity constants of two and four protolytic forms of fluorescein. A possible advantage of the Kubista et al. method is that it mixes a soft modeling approach with a hard modeling approach. This might be best and more general strategy, since it can handle different situations, with only a partial knowledge of the chemistry of the system. The physical constraints method calculates spectral profiles, concentrations and equilibrium constants by utilizing equilibrium expressions that related the components.

In this work, we applied the physical constraints approach to determine the acidity constants of PAR in pure water and in different binary methanol–water mixtures. Data analysis was carried out in MATLAB version of the DATa ANalysis (DATAN) program that was developed by Kubista group.

2. Theory

The theory and application of the physical constraints method was discussed by Kubista et al., in several papers [13–22]. However, the general principal will be outlined briefly.

Spectra of PAR at different pH values are digitized and arranged in a data matrix A, which is decomposed into an orthonormal basis set by NIPALS or any equivalent method [13]:

$$A = TP' + E \approx TP' = \sum_{i=1}^{r} t_i p_i' \tag{1}$$

where the orthogonal target vectors t_i and orthonormal projection vectors p_i' are mathematical constructs that cannot be directly related to component spectra and concentrations, r is the number of independent spectroscopic components, which corresponds to the number of light-absorbing chemical species. It is determined by visual inspection of the t and P' vectors or by performing statistical methods, such as, χ^2-test [23–25]. E is an error matrix.

By assuming linear responses, the spectra in matrix A are linear combinations of the concentrations, C, and spectral responses, V, of the chemical components.

$$A = CV + E \approx CV \tag{2}$$

If the spectral profiles of the components are known, the concentration of each component can easily be

calculated, for example, by least squares minimization. If standards are not available the common belief has been that the components' spectral responses cannot be separated, which precludes their identification. This is due to ambiguity in determining the rotation matrix, R, in the following equations; from Eqs. (1) and (2) follows that there is a square matrix R ($r \times r$) that satisfies

$$T = CR \qquad (3a)$$

$$P = R^{-1}V \qquad (3b)$$

Since $A = CV = C(RR^{-1})V = (CR)(R^{-1}V) = TP'$. If R can be determined, the spectral responses V and concentrations C of the components can be calculated from the target T and projection P' matrices:

$$C = TR^{-1} \qquad (4a)$$

$$V = RP' \qquad (4b)$$

The thermodynamic expression that describes the components' concentration is the main constraint used to determine R, from which thermodynamic parameters and components' spectral responses and concentration are calculated. Therefore, the strategy for determining the rotation matrix R is as follows. Concentrations of the chemical species are calculated from the equilibrium expressions for various trial values of the equilibrium constants, and are fitted to the calculated target vectors according to Eq. (3a). The accuracy of this fit depends crucially on the trial values of the equilibrium constants, and best fit determines their values and the elements of matrix R.

3. Experimental section

Extra pure methanol (MeOH, Fluka) was used as received. Triply distilled deionized water was used throughout. Reagent grade 4-(2-pyridylazo)resorcinol (PAR) (Merck), sodium hydroxide (Merck), succinic acid (Merck), oxalic acid (Merck), lithium hydroxide (Merck) and potassium nitrate (Merck) were of the highest purity available and used without further purification.

All spectra were recorded on a CECIL 9050 spectrophotometer. Measurements of pH were made with a Metrohm 692 pH meter using a combined electrode.

In all experiments, the ionic strength of the solutions used was kept constant at 0.1 M using potassium nitrate as the supporting electrolyte.

To calibrate the pH meter in various binary methanol–water mixtures used, the 0.01 M solutions of oxalate and succinate buffers were employed. The reference values of pH of these buffer solutions in different methanol–water mixtures have been reported previously [26].

4. Results and discussion

The electronic absorption spectra of PAR in binary solvent mixtures at various pH values at 400–600 nm intervals were recorded. Sample spectra of PAR at different pH values in pure water and 90% (w/w) of methanol to water are shown in Figs. 1 and 2, respectively.

The principal component analysis of all absorption data matrix obtained at various pH shows at least four significant factors. This claim is, also, supported by the statistical indicators method that has been recently developed by Elbergali et al. [27], which has predicted four distinguishable components in the samples. These factors could be attributed to the three dissociation equilibria of a triprotic acid such as PAR. This may not be concluded by inspection of visible spectra of PAR.

The pK_a values of PAR were investigated in 10 different methanol–water binary mixtures spectrophotometrically at 25 °C. Acidity constants of PAR in several mixtures were evaluated using DATAN program using the corresponding absorption spectra–pH data. From inspection of the experimental spectra it is hard to guess even the number of protolytic species involved. The calculated four most significant projection vectors, P', with clear spectral features, as compared to noise, evidencing 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.

Output of DATAN program is pK_a values, number of principal components, projection vectors (loadings), concentration distribution diagrams and 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
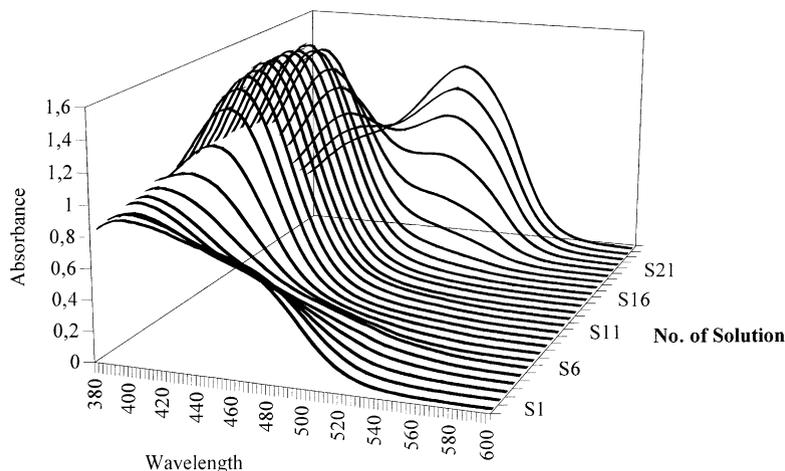
Fig. 1. Absorption spectra of PAR in pure water at different pH values: (1) 2.01, (2) 2.56, (3) 3.00, (4) 3.51, (5) 4.02, (6) 4.50, (7) 5.00, (8) 5.50, (9) 6.00, (10) 6.50, (11) 7.03, (12) 7.49, (13) 8.00, (14) 8.51, (15) 9.02, (16) 9.54, (17) 9.78, (18) 10.27, (19) 10.72, (20) 11.22, (21) 11.60, (22) 12.00, (23) 12.41, (24) 12.81, (25) 13.21, (26) 13.67.

all solvent mixtures. There is a good agreement between the obtained results for pK_a values in this work and previously reported values [28]. One of the very important output of DATAN is calculated spectrum of different forms of PAR at each solvent mixture.

The calculated spectra at different solvent mixture are shown in Fig. 3. It is interesting to note that, the nature of the solvent composition has a fundamental

effect on each pure spectrum. As it is clear from the Fig. 3, this effect is more for H_3L^+ and HL^- than H_2L and L^{2-}. The spectrum of H_3L^+ species has a λ_{max} at 480 nm and a shoulder about 400 nm. The solvent effect on this spectrum is very interesting. As the weight percent of MeOH goes up, the absorption intensity at 480 nm decreased and increased at 400 nm. This can be described using the nonelectrostatic (H-bonding) property on the stabilization and/or destablization of ground and excited state of n $\rightarrow$ p* and p $\rightarrow$ p* transitions.

The most important features of distribution diagrams are the pH limit of evolving and disappearance

Fig. 2. Absorption spectra of PAR in 90% (w/w) methanol to water binary mixture at different pH values: (1) 1.63, (2) 2.06, (3) 2.57, (4) 3.54, (5) 4.11, (6) 4.66 (7) 5.06, (8) 5.57, (9) 6.10, (10) 6.57, (11) 7.12, (12) 7.68, (13) 8.11, (14) 8.57, (15) 9.05, (16) 9.56, (17) 10.09, (18) 10.54, (19) 11.77, (20) 11.59, (21) 12.01, (22) 12.55, (23) 13.09, (24) 13.52, (25) 13.88. Spectral data of Fig. 2.

Table 1
Acidity constants of PAR in different methanol + water mixtures

Methanol (wt.%)	Acidity constants		
	pK_{a_1}	pK_{a_2}	pK_{a_3}
90	2.45	6.82	12.77
80	2.50	6.69	12.68
70	2.57	6.52	12.57
60	2.65	6.35	12.45
50	2.72	6.28	12.40
40	2.80	6.11	12.37
30	2.88	5.97	12.22
20	2.90	5.86	12.21
10	3.01	5.80	12.11
0	3.07	5.50	12.04
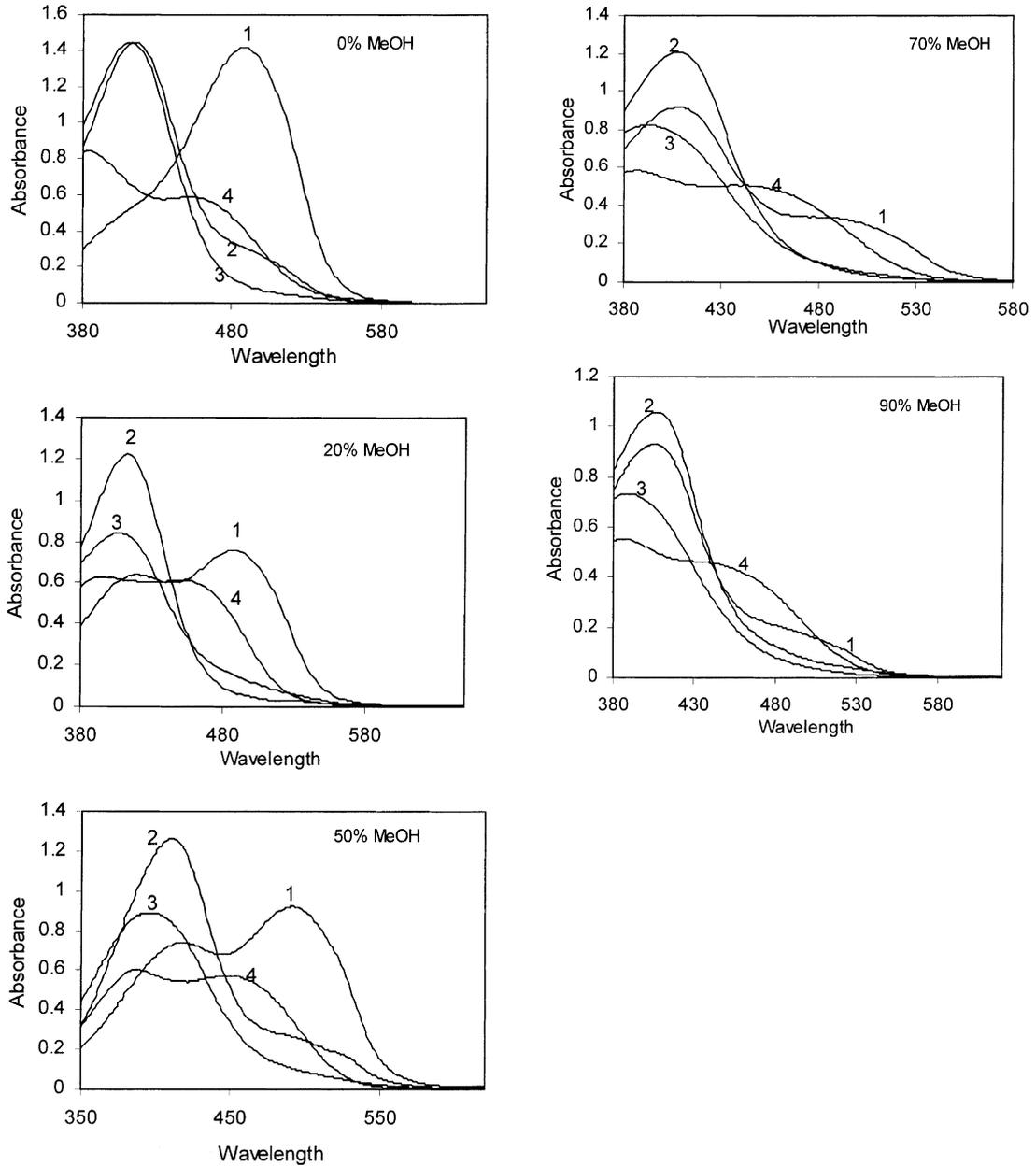
Fig. 3. The pure absorption spectra of different form of PAR, H_3L^+ (1), H_2L (2), HL^- (3), L^{2-} (4).

of components. So according to distribution diagrams it is may conclude that the spectra at smaller pH than 2.5 assigned to H_3L^+ form because this form is dominated at this range. At pH 3–5.5 interval the H_2L form is dominated and hence the

spectra mostly attributed to this form. The HL^- and L^{-2} forms appeared at pH intervals 6–12.5 and pH $>$ 12.5, respectively. Samples of obtained distribution diagrams are shown in Figs. 4 and 5.
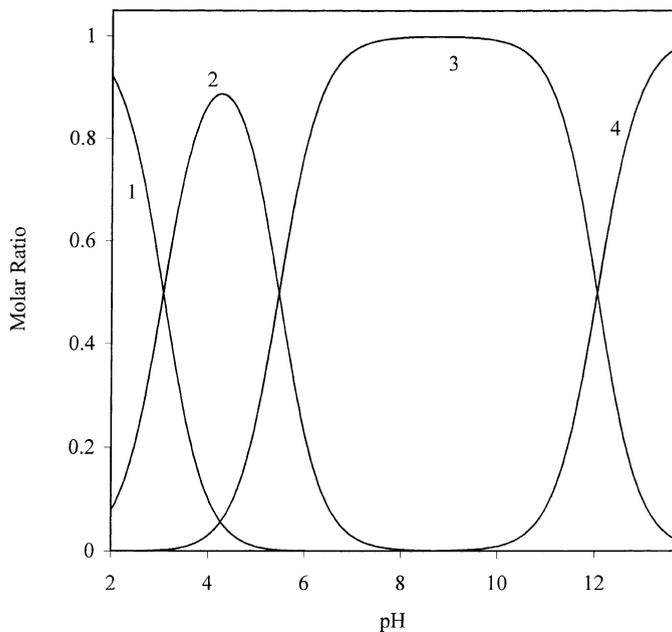
Fig. 4. Distribution of major species of PAR, H_3L^+ (1), H_2L (2), HL^- (3), L^{2-} (4), as a function of pH for the spectral data of Fig. 1.
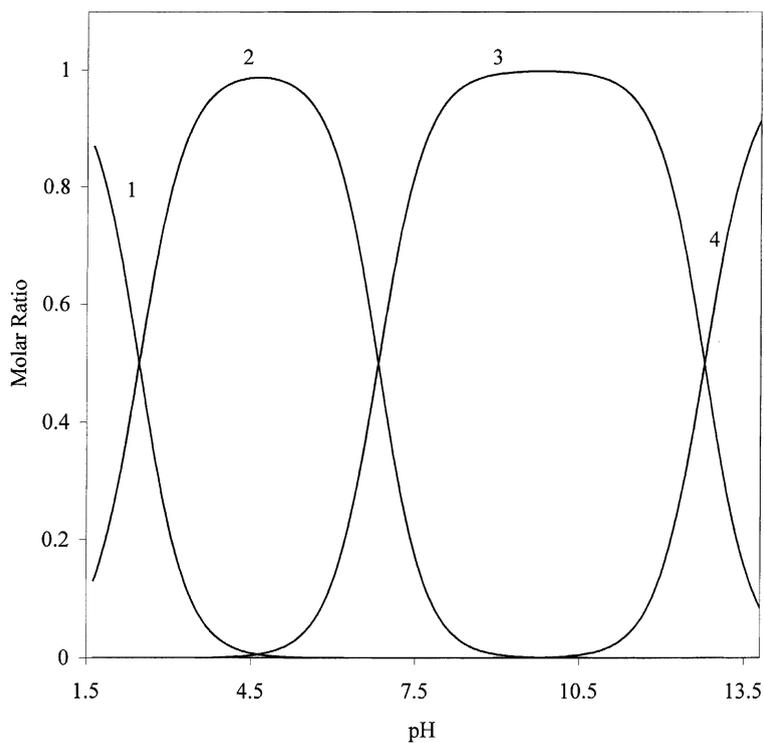
Fig. 5. Distribution of major species of PAR, H_3L^+ (1), H_2L (2), HL^- (3), L^{2-} (4), as a function of pH for the spectral data of Fig. 2.

The data shown in Table 1 clearly illustrate the important influence of the nature of the solvent on the dissociation reaction. Acidity constants of second and third step of dissociation of PAR decreases with increasing the mole fraction of methanol in the mixed solvents. It has been shown that the solvating ability [29] (as expressed by the Gutmann 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, [30] and dielectric constant $\varepsilon = 78$) which can dissociate the acid and stabilize the produced anion and hydrogen ion. Thus, it is expected that addition of methanol with lower donor number and dielectric constant (DN = 19, $\varepsilon = 32.6$) to water decreases the extent of interaction between the acid anion and proton with solvent, and this decreases the acidity constants of acid.

It is interesting to note that there is actually a linear relationship between the pK_a of three dissociation steps (first step decreases and second and third steps

increases) and the mole fraction of methanol (X_{MeOH}) in the binary mixed solvents used in Fig. 6. The same trend has already been reported for various organic molecules in different solvent mixtures [1,2]. 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 the 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 is decreased, more energy will be required to separate the anion and cation and consequently the extent of dissociation of acid will be lowered. Therefore, the increase in first step and the decrease in second and third step
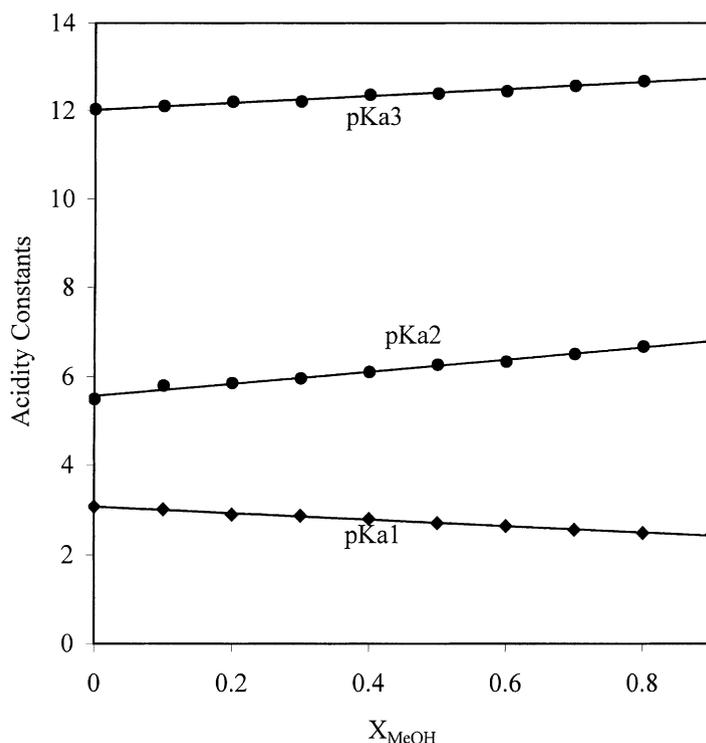
Fig. 6. Variation of acidity constants values of PAR with X_{MeOH} in binary mixtures.

of dissociation constants is due to increasing the mole fraction of methanol in the binary mixed solvent.

References

[1] D. Almasifar, F. Forghaniha, Z. Khojasteh, J. Ghasemi, H. Shargi, M. Shamsipur, J. Chem. Eng. Data 42 (1997) 1212.

[2] M. Shamsipur, J. Ghasemi, F. Tamaddon, H. Shargi, Talanta 40 (1992) 697.

[3] C.W. Dawies, Electrolytic Dissociation, Butterworths, London. 1962.

[4] H. Baggesgaard-Rasmussen, Z. Analyt. Chem. 105 (1936) 269.

[5] S.R. Palit, Ind. Eng. Chem. Anal. Ed. 18 (1946) 246.

[6] L. Chmurzynski, Z. Warnke, Aust. J. Chem. 46 (1993) 185.

[7] F.J.C. Rossotti, H.S. Rossoti, The Determination of Stability Constants, McGraw-Hill, New York, 1961.

[8] L.G. Sillen, B. Warnqvist, Ark. Kemi. 31 (1968) 377.

[9] H. Gampp, M. Maeder, C.J. Mayer, A. Zuberbuhler, Talanta 32 (1985) 95–257.

[10] D.J. Legget, in: D.J. Legget (Ed.), Computational Methods for the Determination of Formation Constants, Plenum Press, New York, 1985, p. 159.

[11] P. Gans, A. Sabbatini, A. Vacca, Talanta 43 (1996) 1739–1753.

[12] W. Lawton, E. Sylvestre, Technometrics 13 (1971) 617.

[13] M. Kubista, R. Sjoback, B. Albinsson, Anal. Chem. 65 (1993) 994.

[14] M. Kubista, R. Sjoback, J. Nygren, Anal. Chim. Acta 302 (1995) 121.

[15] J. Ngren, J.M. Andrade, M. Kubista, Anal. Chem. 68 (1996) 1706.

[16] I. Scarmino, M. Kubista, Anal. Chem. 65 (1993) 409.

[17] R. Sjoback, J. Nygren, M. Kubista, Spectrochim. Acta A 51 (1995) L7.

[18] J. Nygren, A. Elbergali, M. Kubista, Anal. Chem. 70 (1998) 4841.

[19] A. Carosena, J.M. Andrade, M. Kubista, Anal. Chem. 67 (1995) 2373.

[20] M. Kubista, R. Sjoback, S. Eriksson, B. Albinsson, Analyst 119 (1994) 417.

[21] M. Kubista, P. Hagmar, P. Nielson, B. Nordn, J. Biomol. Struc. Dyn. 1 (1990) 37.

[22] M. Kubista, Chemometr. Intell. Lab. Syst. 7 (1990) 273.

[23] R. Fisher, W. Mackenzie, J. Agric. Sci. 13 (1923) 311.

[24] H. Wold, in: F. Daved (Ed.), Research Papers in Statistics, Wiley, New York, 1966, p. 441.

[25] K.V. Mardia, et al., Multivariate Analysis, Academic Press, London, 1979.

[26] R.G. Bates, Determination of pH: Theory and Practice, Wiley, New York, 1973.

[27] A. Elbergali, J. Nygren, M. Kubista, Anal. Chem. Acta 379 (1999) 143.

[28] A. Hulanicki, S. Glab, G. Ackerman, Pure Appl. Chem. 55 (7) (1983) 1137.

[29] V. Gutmann, Coordination Chemistry in Nonaqueous Solutions, Springer, New York, 1960.

[30] P.H. Erlich, A.I. Popov, J. Am. Chem. Soc. 93 (1971) 5620.