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Solvent Effects on Tautomeric and Microscopic Protonation Constants of Glycine in Different Aqueous Solutions of 1,4-Dioxane

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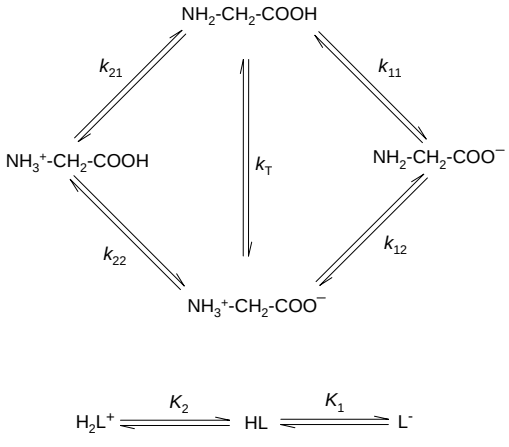
ABSTRACT

The acid-base equilibria of glycine have been studied in different aqueous solutions of 1,4-dioxane (0-50 % by v/v) using potentiometric method. In this study, the macro and micro protonation constants of the amino acid and its tautomeric constant have been determined at 25 °C and constant ionic strength 0.1 mol dm^{-3} (NaCl). The protonation and the tautomeric constants of glycine in different binary mixtures were analyzed in terms of Kamlet, Abboud and Taft (KAT) parameters. Single-parameter correlations of the constants versus α (hydrogen-bond donor acidity), β (hydrogen-bond acceptor basicity) and π* (dipolarity/polarizability) are poor in all solutions. Multi-parameter correlations show better results, but dual-parameter correlations represent significant improvements with regard to the single- and multi-parameter models. Linear correlation is observed when the experimental protonation constant values are plotted versus the calculated ones, while the KAT parameters are considered. Finally, the results are discussed in terms of the effect of the solvent on protonation and tautomeric constants.

Keywords: Glycine; Micro and macro protonation and tautomeric constants; 1,4-Dioxane; Solvent effect

INTRODUCTION

A few efforts have been devoted to determining protonation microconstants of some amino acids using different methods [1-5]. Nevertheless, there is still little information in the literature about the effect of organic solvents (or their aqueous mixtures) on protonation microconstants of amino acids [6]. These results are possibly useful in elucidating the properties and the solute-solvent interactions in these media.
Depending on the pH values of the media, an amphiprotic compound (such as glycine) may exist in four different microforms which are shown in Scheme 1.



Scheme 1. Microscopic and macroscopic dissociation equilibria of glycine.

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Although, the neutral form of an amino acid is more lipophilic and hence more effective in diffusing through the cellular membrane as compared with the charged forms, the macroscopic protonation constants can provide no information about the equilibrium that produces HL^{o} (with no charge) species. The tautomeric and the protonation microconstants can describe the amount of various microforms of an amino acid at different pH values.

Aqueous-organic solvent, mainly 1,4-dioxane, have been widely used due to sparingly or insolubility of many compounds in pure water as solvent. Further, any physicochemical property of solution can be easily varied by changing the compositions of water or the organic solvent in the mixtures. However, chemists have usually attempted to understand solvent effects in terms of polarity, defined as the overall solution capabilities that depend on all possible (specific and non-specific) intermolecular interactions between solute and solvent molecules. Many reports on solvent polarity scales have been published in the last few decades [7]. Previously, the solvent effect on the protonation equilibrium was believed to be guided chiefly by electrostatic interactions (Born model) [11]. However, recent studies have revealed that the change in macroscopic properties such as the dielectric constant of the solvent cannot be the sole factor [7]. 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.

In continuation of our previous work [9-15], in this study the protonation microconstants of glycine (the simplest amino acid) have been determined in different aqueous-1,4-dioxane mixtures to examine the dependence of acid-base equilibria on solvent composition.

EXPERIMENTAL

Chemicals

All materials were analytical reagent grade. Glycine, ($C_2H_5O_2N$ 99.8 %) and glycinemethylester ($C_3H_7O_2N$, 99.5 %) were obtained from Merck and used as received. The NaOH solution was prepared from titrisol solution (Merck). hydrochloric acid was supplied from Merck and was used without further purification. Sodium chloride (Merck, 99.5 %) was kept at room temperature in vacuum at least 72 hours before use. 1,4-dioxane was obtained from Merck and was used without further purification. All dilute solutions were prepared from double-distilled water with a specific conductance equal to 1.3 ± 0.1 μS cm^{-1}.

Apparatus

The electromotive force, E, was measured using a pH meter Precisa model 960. The combined glass-pH electrode (model 6.0258.000) was modified by replacing its aqueous KCl solution with 0.1 mol dm^{-3} NaCl saturated with AgCl. The electrode was soaked for (15 to 20) minutes in a water-alcohol mixture before the potentiometric measurements. All titrations were carried out in a 80 mL thermostated double-walled glass vessel. To exclude carbon dioxide from the system, a stream of purified nitrogen was passed through a sodium hydroxide solution and then bubbled slowly through the reaction solution.

Procedure

All measurements were performed at 25 °C and constant ionic strength 0.1 mol dm^{-3} (sodium chloride). The protonation constants were evaluated from measurements of the emf by titration of a 25 mL glycine or glycine methyl ester $(5.0\text{-}8.0)\times10^{-3}$ mol dm^{-3} solution with a 0.1 mol dm^{-3} sodium

hydroxide solution both in the same ionic strength and mole fraction of organic solvent of 1,4-dioxane [(0 - 50) % by v/v].

RESULTS AND DISCUSSION

Macroscopic and Microscopic Protonation Constants

The macroscopic and microscopic protonation equilibria of glycine are shown in Scheme 1. Depending on pH of the solution, the amino acid could exist in four different microforms which are cationic (H_2L^+), zwitterionic ($HL^{\pm}$), neutral (HL^o), and anionic (L^-) species. In order to determine the protonation micro constant the knowledge of the macro constants, K_1 and K_2, values are necessary. These constants are expressed by Eqs 1-3:

$$[HL] = [HL^{\pm}] + [HL^o] \quad (1)$$

$$K_2 = ([HL^{\pm}] + [HL^o])[H^+]/[H_2L^+] \quad (2)$$

$$K_1 = [L^-][H^+]/([HL^{\pm}] + [HL^o]) \quad (3)$$

Where the total concentration of zwitterionic and neutral species ($[HL^{\pm}] + [HL^o]$), are not distinguishable by acid-base titration. The microscopic (k_{11}, k_{12}, k_{21}, k_{22}) and tautomeric (k_T) constants may be written as:

$$k_{11} = [L^-][H^+]/ [HL^o] \quad (4)$$

$$k_{12} = [L^-][H^+]/ [HL^{\pm}] \quad (5)$$

$$k_{21} = [HL^o][H^+]/[H_2L^+] \quad (6)$$

$$k_{22} = [HL^{\pm}][H^+]/[H_2L^+] \quad (7)$$

$$k_T = [HL^o]/[HL^{\pm}] \quad (8)$$

To obtain microscopic constants of an amino acid, one of the micro constants have to be measured independently. To do this the most popular method that has been employed before for determination of some microscopic constants is used in this work. In this method the carboxylic acid function of the amino acid is usually alkylated by a methyl (or an ethyl) group which is believed that this group has the same electronic influence on the molecule as does the proton that it replaces [16-18].

The protonation constant values of glycine were determined potentiometrically by titration of appropriate solutions of the amino acid in the water-dioxane mixtures studied. In this way, glycine was fully protonated at the beginning of a titration by adding a certain amount of hydrochloric acid at first and then using sodium hydroxide solution (0.1 mol dm^{-3}) as titrant. The protonation constants were obtained from systematic emf measurements of the following cell: GE/HCl-NaCl, H_2L^+ + HL + L^- in water-dioxane /HCl-NaOH/Ag-AgCl, where GE is the glass electrode and H_2L^+, HL and L^- are the different species of the amino acid involved in the protonation equilibria studied.

The fraction of protons still bound to the amino acid, $\bar{n}$, can be written as

$$\bar{n}_{cal} = (C_H - [H^+]) / C_L \quad (9)$$

where C_H and C_L are the total concentrations of protons and the amino acid, respectively. Substituting $C_L = [H_2L^+] + [HL] + [L^-]$ and $C_H = [H^+] + [HL] + 2[H_2L^+]$ in eq 9, leads to

$$n_{cal} = ([HL] + 2[H_2L^+]) / ([L^-] + [HL] + [H_2L^+]) \quad (10)$$

substituting the protonation constants instead of concentration of the different species of glycine in eq 10, rearranging and cancelling like terms, it gives

$$\bar{n}_{cal} = (K_1[H^+] + 2K_1K_2[H^+]^2) / (1 + K_1[H^+] + K_1K_2[H^+]^2) \quad (11)$$

where K_1 and K_2 represent the protonation constants of the amino and carboxylic acid groups of the amino acid, respectively. On the other hand, electrical neutrality demands that the concentration of the cations should equal the concentration of the anions at all times during a titration, and hence

$$n_{exp} = (C_L + [Cl^-] - [Na^+] - [H^+] + [OH^-]) / C_L \quad (12)$$

In eqs 11-12, $[Na^+]$ originates from the titrant used (NaOH and NaCl), $[Cl^-]$ is introduced from the hydrochloric acid and

NaCl added, and $[H^+] = 10^{(Ecell - E'a) / k}$ and $[OH^-] = K_{ap}/[H^+]$ (K_{ap} is the autoprotolysis constant). Using a suitable computer program (Microsoft Excel Solver) [19] the data from eqs 11-12 were fitted for estimating the protonation constant values of glycine in different aqueous solutions of the dioxane. We used the Gauss-Newton nonlinear least-squares method in the computer program to refine the $\bar{n}$ values by minimizing the error squares sum from eq 13.

$$U = \sum(\bar{n}_{exp} - \bar{n}_{cal})^2 \qquad (13)$$

where $\bar{n}_{exp}$ is an experimental $\bar{n}$ and $\bar{n}_{cal}$ is the calculated one.

The four microscopic protonation constants of glycine could be calculated from the macroscopic protonation constants of the amino acid if the value of only one microscopic constant (for example k_{21}) was available. The value of k_{21} was determined from measurement of glycine methyl ester with this assumption that the protonation constant of the compound is the same as that of k_{21} (the uncharged form) for the amino acid. This assumption is the best approximation available in the literature for this purpose [17, 20]. So, the values of k_{11}, k_{12}, k_{22}, and k_T have been calculated as:

$$K_2 = k_{21} + k_{22} \qquad (14)$$
$$1/K_1 = 1/k_{11} + 1/k_{12} \qquad (15)$$
$$k_T = k_{21}/k_{22} = k_{12}/k_{11} \qquad (16)$$

The calculated macro and micro protonation constant values of glycine in different water-dioxane mixtures are listed in Tables 1 and 2 together with the values reported in the literature for comparison [21-22]. The protonation constant values obtained in this work are in good agreement with those reported before. The little differences are due to the different experimental method and the fact that a different background electrolyte has been employed to determine the values.

In Figure 1, the equilibrium distribution of various species of glycine in water is shown as a function of pC_H. The calculations are based on the protonation constant values given in Table 1.

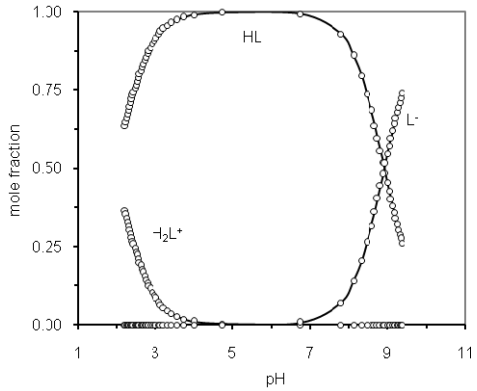

Fig. 1. Distribution diagram of the different species of glycine in water at 25 °C and an ionic strength of 0.1 mol dm^{-3} (NaCl).

Table 1. Protonation constants of the carboxylic, K_2, and the amino, K_1, groups of glycine at 25 °C, different aqueous solutions of 1,4-dioxane, and an ionic strength of 0.1 mol dm^{-3} (NaCl), together with some values reported in the literature

1, 4 dioxane % (v/v)	log K_1	log K_2
0.0	2.01	9.04
10	2.04	8.94
20	2.29	8.87
30	2.44	8.81
40	2.60	8.75
50	2.68	8.68

Solvent effect

The two macroscopic protonation constants of glycine in water-dioxane mixed solvents have different behavior (Table 1). The protonation constant of the amino group of the amino acid, K_1, increased as the solvent became enriched in the organic component, but the protonation constant of the carboxylic acid group, K_2, decreased as the organic solvents increased in the mixture. It is very difficult to interpret the variation of the protonation constant values of glycine with respect to the percentage of the organic

solvents in the mixtures using the dielectric constant of the solutions as a single parameter.

In general, the standard free energy of protonation equilibria consists of two terms: an electrostatic term, which can be estimated by the Born equation [23-24] and a non-electrostatic term, which includes specific solute-solvent interactions. When the electrostatic effects predominate, then in accordance with the Born equation, eq 17, a plot of log K versus the reciprocal of the dielectric constant of the media, ε, should be linear.

$$\Delta \log K = (121.6z/r)(1/\varepsilon - 0.0128) \qquad (17)$$

where r is the common radius of the ions and z is the square summation of the charges involved in the protonation equilibria. For example z = 2 for the charge type $L^- \rightleftarrows HL$ and z = 0 for the charge type $HL \rightleftarrows H_2L^+$.

The correlation between log K_2 with the reciprocal of the dielectric constant of water-dioxane solvent mixture is linear, with correlation coefficients more than 0.91 (Fig. 2). However, there is no change in the number of charges involved in the protonation equilibria of the zwitterionic form of glycine, K_1. In this case, the correlation between log K_1 values and 1/ε is poor (Fig. 2) and so the protonation possibly depends on the solute-solvent interaction of the different species in the mixtures.

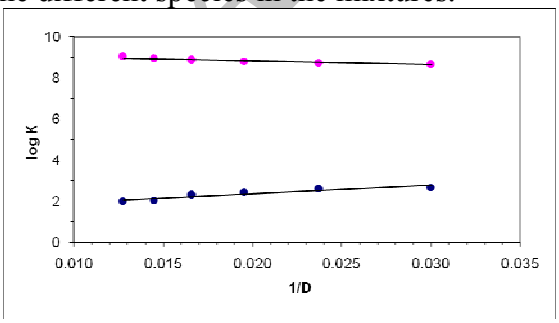

Fig. 2. Plots of the experimental values of log K_2 and log K_1 versus the reciprocal of the dielectric constant of different mixed solvents at 25 °C and an ionic strength of 0.1 mol dm^{-3} (NaCl).

The values of log K_1 and log K_2 of the amino acid show small changes in the range 0 to about 20 % (v/v) of 1,4-dioxane and a larger increase when the mixture is richer in the organic solvents. This variation with the percentage of the organic solvent is due to the solute-solvent interaction effects. This effect possibly changes the structure of the mixtures [24]. In fact, the water structure remains intact in the water rich region and the 1,4-dioxane molecules occupy the cavities between water molecules without changing the water structure [24]. In this region there are small changes in the protonation constants of glycine. However, the protonation constant values change by larger amounts when the percentage of the organic solvents increases to higher values. In this region the influence of 1,4-dioxane on water structure is high and the solute-solvent interactions cause a greater variation in log K_1 and log K_2 values. This discussion is in accordance with previous results for other aqueous-organic solvent mixtures and in agreement with the present results [23-26]. Furthermore, the protonation constants of the amino acid have different values in the mixed solvent system studied in the same percentage of organic solvent in the mixtures. This should be due to the difference in the dielectric constant values of the mixture. These findings necessitate elucidating the nature of solute-solvent interaction for a better understanding of solvent effects.

To obtain a quantitative method for evaluation of the solute-solvent interaction on protonation constants, we used the method introduced by Kamlet, Abboud and Taft (KAT) [27-28]. The KAT equation contains non-specific as well as specific solute-solvent interactions separately, and that the latter could be subdivided into solvent Lewis- acidity interactions (hydrogen-bond accepter, HBA solute, and hydrogen-bond donor, HBD solvent) and solvent Lewis-basicity interactions (HBD solute-HBA solvent). In general, all of these parameters constitute more comprehensive

measures of solvent polarity than the dielectric constant or any other single physical characteristic alone, because they reflect more reliably the complete picture of all intermolecular forces acting between solute and solvent molecules. In general, this approach has been widely and successfully applied in the correlation analysis of all kinds of solvent-dependent processes [7]. The multiparametric equation 18, has been proposed, using the solvatochromic solvent parameters, α, β and π* which have been introduced in previous reports [7, 9-15].

$$\log K = A_0 + a\alpha + b\beta + p\pi^* \qquad (18)$$

where A_0 represents the regression value, π* is the index of the solvent dipolarity/ polarizability, which is a measure of the ability of a solvent to stabilize a charge or a dipole by its own dielectric effects. The π* scale was selected to run from 0.0 for cyclohexanone to 1.0 for dimethylsulfoxide. The α coefficient represents the solvent hydrogen-bond donor (HBD) acidity, in other words it describes the ability of a solvent to donate a proton in a solvent to a solute hydrogen-bond. The α scale extends from 0.0 for non-HBD solvents to about 1.0 for methanol. The β coefficient is a measure of a solvent hydrogen-bond acceptor (HBA) basicity, and describes the ability of a solvent to accept a proton in a solute to solvent hydrogen-bond. The β scale was selected to extend from 0.0 for non-(HBA) solvents to about 1.0 for hexamethyl phosphoric triamide.

The regression coefficients a, b and p measure the relative susceptibilities of the solvent-dependence of log K to the indicated solvent parameters. In order to explain the determined log K values through the KAT solvent parameter, the protonation constants were correlated with the solvent properties by means of single and multiple regression analysis by a suitable computer program (Microsoft Excel Solver and Linest) [19]. We used the Gauss-Newton non-linear least-squares method in the computer program to refine the log K by minimizing the error squares sum from eq 19.

$$U = \sum(\log K_{exp} - \log K_{cal})^2 \qquad (19)$$

The procedure used in the regression analysis involves a rigorous statistical treatment to find out which parameter in eq 18 is best suited to the water-organic mixed solvents. So, a stepwise procedure and least-squares analysis were applied to select the significant solvent properties to be influenced in the model and to obtain the final expression for the protonation constants. Therefore, the KAT equation, eq 18, was used as single- and multi-parameters for correlation analysis of log K in various solvent mixtures. The computer program used can give the values of A_0, a, b, p and some statistical parameters including the r^2 coefficient, the uncertainty value of any parameter (given in brackets) and the overall standard error (ose) of log K. The KAT parameters and the dielectric constant values for all the water-1,4-dioxane mixtures used in this work were obtained from the plot of each property versus the mole fraction of the organic solvent of the values that were reported in the literature for some other percentages of aqueous solutions of methanol [26-29], those are listed in Table 4. Although the solvent polarity is identified as the main reason of the variation of log K values in water-organic solvent mixtures, but the results show any single-parameter correlations of log K_1 and log K_2 values individually with □*, α, and β did not give good results in all cases. However, the correlation analysis of log K_1 and log K_2 values with dual-parameter equations indicate significant improvement with regard to the single- or multi-parameter models. The expressions of the KAT equation for each property are obtained and are given as dual-parameters (including β and π*) as follows, the uncertainty values for each term

in eq 20 are shown in bracket using the Linest program.

$\log K_1 = 11.02(\pm 0.95) - 3.36(\pm 0.85)\ \beta - 0.31(\pm 0.47)\pi^*$ (20a)

($N = 6$, $r^2 = 0.986$, ose $= 1.95\times10^{-2}$)

$\log K_2 = -2.33(\pm 2.21) + 7.22(\pm 1.97)\beta + 0.66(\pm 1.09)\pi^*$ (20b)

($N = 6$, $r^2 = 0.984$, ose $= 4.53\times10^{-2}$)

The coefficients of β and π* in eqs 20a and 20b are different from each other and are in the order of $\beta > \pi^*$. This indicates the hydrogen- bond acceptor basicity parameter plays a major role in all cases and the polarity parameter of the solvent has less significance in the correlation analysis of K_1 and K_2 in the variation of macroscopic protonation constant values of glycine in the proposed various aqueous solutions of 1,4-dioxane.

If the dielectric constant of the media was the only factor for the solvent effect on protonation, it may be expected that the log K in a solution with the higher dielectric constant should be greater than those of all the other aqueous solutions of 1,4-dioxane. It can be seen from Table 4 that the dielectric constants of the solvent mixtures decrease as the solutions are enriched in organic solvent. The values of log K_2 decrease with decreasing the dielectric constant of the media, but this is not true in the case of log K_1 values. It is impossible to explain this variation using the dielectric constant approach as a single parameter. However, a dual-parametric approach according to the KAT equation was applied to find out which parameter is responsible for this behavior. The positive π* coefficients in the correlation analysis of log K_2 by the KAT equation imply that a decrease in the polarity of the mixed solvents, decreases the protonation constant values of the amino group. According to this discussion, the negative π* coefficient obtained for log K_1 represents a decrease in polarity of the solvent mixtures causes an increase in the protonation constant values of the carboxylic acid. This indicates the polarity parameter, π*, is the most important (with a relatively larger difference with the acceptor basicity parameter) in the correlation analysis of the protonation constants of glycine. In a previous work, in correlation analysis of the protonation constants of cysteine in aqueous solutions of methanol, almost the same results were obtained [25]. Furthermore, the positive coefficient β in the correlation of log K_2 and negative in the case of log K_1 suggests that the increasing acidity of the solvent mixtures decreases the protonation constant of the carboxylic acid group of glycine and increases the protonation constants of the amino group of the amino acid. This could be due to the charges involved in the protonation equilibria. An increase in the acidity of the mixtures increases the solvation of the cationic species of glycine, and therefore makes protonation equilibrium more likely. However, this is not true in the case of K_1 that has a negative coefficient β.

The protonation micro constants of glycine in water-dioxane mixed solvents again have different behaviors. log k_{21}, log k_{12} and log k_T decrease, but log k_{22} and log k_{11} increase with increasing the proportion of organic solvents in the mixtures, Table 2. This behavior can be interpreted considering the previous discussion about the macroscopic protonation constants and the fact that the cationic and anionic species are more solvated in alkaline and acidic media, respectively. However, the decreasing of log k_{22} values ($[H_2L^+]/[HL^o][HL]$) with increasing the amount of ether in the mixed solvents is possibly due to the existence of a preferential solvation of the neutral form of glycine in water-rich region [6]. But this is not true for the zwitterionic form of the amino acid. Therefore, log k_{21} ($[H_2L^+]/[HL^0][H^+]$) values increase with increasing the proportion of ether in the mixed solvents.

Table 2. The microscopic protonation and tautomeric constant values of glycine at 25 °C, different aqueous solutions of 1,4-dioxane, and an ionic strength 0.1 mol dm^{-3} (NaCl)

1,4-dioxane % (v/v)	log k_{21}	log k_{22}	log k_{11}	log k_{12}	log k_T
0.0	7.76	2.01	3.29	9.04	3.86
10	7.65	2.04	3.33	8.94	3.75
20	7.59	2.29	3.57	8.87	3.31
30	7.44	2.44	3.81	8.81	3.05
40	7.34	2.60	4.01	8.75	2.82
50	7.21	2.68	4.15	8.68	2.69

Table 3. KAT solvatochromic parameters and the dielectric constants of different aqueous 1, 4-dioxane mixtures

1,4-dioxane % (v/v)	α [a]	β [a]	π^* [a]	ε [b]
0	1.23	0.49	1.14	78.30
10	1.06	0.51	1.12	69.23
20	0.92	0.54	1.09	60.19
30	0.82	0.56	1.05	51.14
40	0.77	0.59	0.99	42.14
50	0.73	0.61	0.92	33.32

[a] The values are from reference 26.
[b] The values are from reference 29.

In general solute-solvent and solvent-solvent interactions in mixed solvents are more complex than in a pure solvent due to the preferential solvation. These interactions can create new mixed solvent entities in the solvation shell of the solute molecules whose properties and their structures are distinct and different from those in pure solvent. In this case, the molecules of solute can usually interact to different degrees with each solvent component. The important consequence of diversity in these interactions is that the composition of solvation shell in the vicinity of solute (local composition) differs from that of the bulk composition of the mixed solvent. Therefore a specific feature of solvation in the mixture of solvents emerges as a result of the phenomenon which is termed as preferential solvation.

However, the log k_{12} ($[HL^{\pm}]/[L^-][H^+]$) and log k_T ($[HL^{\pm}]/[L^-]$) values decrease with increasing the percentage of dioxane in the mixtures. This can be explained by the fact that dipolar ion is solvated less than the anionic species in the media with higher dioxane content. But the increasing of log k_{11} ($[HL^o]/[L^-][H^+]$) values in the dioxane - rich region are possibly due to the more solvation of the neutral form of the amino acid than the anionic species.

To confirm the validity of above discussion, we again used the KAT equation. The results show any single-parameter correlations of the protonation micro constants (in logarithm scale) values individually with π^*, α, and β did not give good results in all cases. However, the correlation analysis of the values with dual-parameter equations indicates significant

improvement with regard to the single- or multi-parameter models. The expressions of the KAT equation for each property are obtained and are given as dual-parameters (including β and π*) as follows, the uncertainty values for each term in eq 21 are shown in bracket using the Linest program.

$\log k_{21}$ (dio) = 8.03(±1.39) -2.76(±1.24) β + 0.94(±0.68)π* (21a)

$\log k_{22}$ (dio) = -2.33(±2.21) + 7.22(±1.97) β + 0.66(±1.09)π* (21b)

$\log k_{11}$ (dio) = 0.67(±2.78) +6.62(±2.48) β - 0.59(±1.36)π* (21c)

$\log k_{12}$ (dio) = 11.02(±0.95) -3.36(±0.85) β – 0.31(±0.47)π* (21d)

$\log k_T$ (dio) = 13.70(±3.20) -14.53(±2.58) β – 2.34(±1.57)π* (21e)

The coefficients of π* in eqs 21a to 21e are much lower than β (the coefficients of β have very minor effect and so they are not considered further in this section). This indicates the hydrogen- bond acceptor basicity parameter plays a major role in all cases and the polarity parameter of the solvent has very less significance in the correlation analysis of the variation of microscopic protonation constant values of glycine in the proposed various aqueous solutions of 1,4-dioxane.

The positive π* coefficients in the correlation analysis of $\log k_{22}$, $\log k_{11}$, and $\log k_T$ by the KAT equation imply that a decrease in the polarity of the mixed solvents, decreases the protonation micro constant values of the amino acid. According to this discussion, the negative π* coefficient obtained for $\log k_{21}$ and $\log k_{12}$ represents a decrease in polarity of the solvent mixtures causes an increase in the protonation micro constant values of glycine.

CONCLUSIONS

Due to the fact that amino acids are widely applied in many chemical and biochemical fields, it is essential to characterize their properties in terms of the microconstants. These give useful information about elucidation of numerous biological compounds like proteins, enzymes, etc. Furthermore, the microscopic protonation constants of different amino acids not only are used for quantitative purposes but also can be used to evaluate the solvent effect on such compounds.

In this work, the tautomeric and micro and macro protonation constants of glycine were analyzed in different aqueous 1,4-dioxane mixtures using Kamlet, Abboud and Taft parameters. Considering the KAT parameter, dual-parameter (β and π*) correlations represent significant improvements with regard to the single- and multi-parameter models and a linear correlation was observed when the experimental protonation constant values were plotted versus the calculated ones. Finally, the results were discussed in terms of the effect of the solvent on protonation and tautomeric constants.

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