Journal of Physical and Theoretical Chemistry
of Islamic Azad University of Iran, 12 (1) 19-31: Spring 2015
(J. Phys. Theor. Chem. IAU Iran)
ISSN 1735-2126

Solvent effects on protonation and complexation of histidine with molybdenum (VI) at different aqueous solutions of methanol

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Received February 2015; Accepted February 2015

ABSTRACT

The formation constants of the species formed in the systems H^+ + Mo(VI) + histidine and H^+ + histidine have been determined at different aqueous solutions of methanol (0 - 45 % v/v) at 25 °C and constant ionic strength (0.1 mol dm^{-3} sodium perchlorate), using a combination of spectrophotometric and potentiometric techniques. The composition of the complex species was determined by the continuous variations method (Job). It was shown that molybdenum (VI) forms a mononuclear 1:1 complex with histidine of the type MoO_3L^- at pC_H 5.8. The protonation of histidine and the formation constant of the formed complex species in various media were analyzed in terms of Kamlet, Abboud, and Taft (KAT) parameters. Single-parameter correlation of the formation constant versus α (hydrogen-bond donor acidity), β (hydrogen-bond accepter basicity) and π^* (dipolarity/polarizability) are poor in all solutions, but dual-parameter correlation represents significant improvement with regard to the single or multi-parameter models. Linear correlation is observed when the experimental log K_S values are plotted versus the calculated ones while the KAT parameters are considered. Finally, the results are discussed in terms of the effect of solvent on protonation and complexation.

Keywords: Molybdenum (VI); Histidine; Protonation and formation constants; Solvent effect.

INTRODUCTION

Many chemical reactions of experimental and practical processes occur in solution. In a variety of chemical fields such as chemical synthesis, solvent extraction, liquid chromatography, chemical kinetics, etc, binary solutions of water and organic solvents are used. Aqueous organic solvent, mainly methanol and ethanol mixtures, have been widely used due to the sparingly or insolubility of many compounds in pure water as solvent. Further, any physicochemical property of solutions can be easily varied by changing the compositions of water or the organic solvent in the mixtures.

The initial reports dealing with the influence of solvent in a reaction with solute molecules have been documented since the 19th century [1]. The influence of solvent on solute molecules has been intensively studied, but the problem is far from being completely understood. Chemists have usually attempted to understand solvent effects in terms of

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polarity, defined as the overall solution capabilities that depend on all possible (specific and nonspecific) intermolecular interactions between solute and solvent molecules. However, the acceptance of a single solvent polarity scale as the most appropriate for interpreting any solvent effect has not yet been achieved. Although the exact definition of solvent polarity is still elusive, it seems reasonable to consider that this property is related to the overall solvation capability of the solvent, encompassing all possible specific and nonspecific intermolecular interactions with solute ions or molecules.

Many reports on solvent polarity scales have been published in the last two decades [2]. Previously, the solvent effect on protonation and formation equilibria was believed to be guided chiefly by electrostatic interactions (Born model) [3]. However, recent studies have revealed that the change in macroscopic properties such as the dielectric constant of the solvent cannot be the sole factors [2]. 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 previous publications [4-5] we have shown that the dielectric constant alone (as believed for many years) cannot serve as a quantitative measurement of solvent polarity. This approach is often inadequate, since the dielectric constant regards a solvent as a non-structured continuum, not composed of individual solvent molecules with their own solvent-solvent interaction, and does not take into account specific solute-solvent interactions. In the present work, we have chosen a well understood system [6] to show how the solvents and their mixtures with various polarities affect the formation constant. Further, an attempt is performed to describe the variations of the protonation constants of histidine in different aqueous solutions of methanol. The solvation of amino acids that constitute proteins is closely connected with the stabilizing and destabilizing effects of electrolytes on protein structure. Therefore, the study of protonation and solvation processes of amino acids in various organic media is important to elucidate their connection between the chemical ability and biological activity, as the polarity and activity of water are expected to be lower in an active site cavity of an enzyme than in bulk water [7].

EXPERIMENTAL

Reagents

Methanol, L-histidine, perchloric acid, and sodium molybdate were obtained from Merck as analytical reagent grade materials and were used without further purification. The NaOH solution was prepared from titrisol solution (Merck). Sodium perchlorate was from Merck and was dried under vacuum at room temperature for at least 72 h before use. All dilute solutions were prepared from double-distilled water with a specific conductance equal to 1.2 ± 0.1 $\mu S \cdot cm^{-1}$.

Apparatus

The electromotive force was measured using a Metrohm model 781 pH ion-meter. A combined glass-pH electrode (model 6.0258.000) was modified by replacing its aqueous KCl solution with 0.01 $mol \cdot dm^{-3}$ NaCl + 0.09 $mol \cdot dm^{-3}$ $NaClO_4$ saturated with AgCl. The electrode was soaked for (15 to 20) minutes in a water-organic solvent mixture before the potentiometric measurements. All titrations were carried out in a 80 mL thermostated double-walled glass vessel.

Spectrophotometric measurements were performed on a UV-Vis Shimadzu 2100 spectrophotometer with a Pentium 4 computer and using thermostated matched

10 mm quartz cells. The measurement cell was of the flow type. A peristaltic pump allowed circulation of the solution under study from the potentiometric cell to the spectrophotometric cell, so the absorbance and the emf of the solution could be measured simultaneously. 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 perchlorate-perchloric acid). The protonation constants were evaluated from measurements of the emf by titration of a 25 mL histidine (5.0×10^{-3} mol dm^{-3}) with 0.1 mol dm^{-3} sodium hydroxide solution both in the same ionic strength and mole fraction of methanol [(0 to 45) % by v/v].

In the first step, the electrode system calibration was performed by Gran's method [8]. For this purpose a measured amount of an acidic solution, at the same conditions of temperature, ionic strength and solvent composition to be used in later experiments, was placed in the double-wall thermostated vessel. The electrode was immersed in the solution in the vessel and the acidic solution was titrated with a strong base (0.1 mol dm^{-3} NaOH). The potential was allowed to stabilize after each addition of the titrant and the recorded emf values were then used to obtain $E°$. The procedure was continued to pH ≅ 2. In the second step, 25 mL of an acidic solution (0.01 mol dm^{-3} $HClO_4$) of histidine [$(4.0 \text{ to } 4.5)\times10^{-4}$ mol dm^{-3}] at the same conditions of temperature, ionic strength and solvent composition was titrated with a sodium hydroxide solution (0.1 mol dm^{-3}). In the third step, two solutions of Mo(VI) + histidine have been prepared with the same concentration, but the ionic strength of the first was maintained with sodium perchlorate and that of the second with sodium hydroxide or perchloric acid, both with the same mole fraction of methanol. In all solutions, the total concentration of the amino acid and the metal ion was kept constant, $[MoO_4^{2-}]$ + [amino acid] = 2.0×10^{-3} mol dm^{-3}. The first solution was then titrated with the second one. The emf was measured after addition of a few drops of the titrant, and the procedure extended up to the required emf. The absorbance of the first solution was then measured when equilibrium was achieved. The procedure was repeated with different solutions of Mo(VI) and the amino acid by varying the mole fraction of Mo(VI) in the range 0 to 1 with constant total concentration of the metal ion and the ligand in solution. In all cases, the procedure was repeated at least three times, and the resulting average values and corresponding deviations from the average are shown in the text and Tables.

The recorded emf values were then converted to pC_H (- log $[H^+]$) using the method was described in the literature [9]. In acidic solution, the measured potential of the cell, E_{cell}, glass elec. / $HClO_4$, $NaClO_4$ (0.1 M), water-methanol // NaCl (0.01 M), $NaClO_4$ (0.09 M) / AgCl, Ag, can be written as

$$E_{cell}(mV) = E°_{cell} + k\log [H^+] + k\log \gamma_{H+} + E_{LJ} \quad (1)$$

where $E°_{cell}$ is the standard potential of the cell, E_{LJ} is the liquid junction potential, k = 2.303RT/F in which R, T and F have the usual meaning, and γ_{H+} is the activity coefficient of hydrogen ion, respectively. Difficulties in computing the activity coefficients of hydrogen ion in various aqueous mixtures of organic solvents lead

to the measurement of emf (electromotive force) versus H^+ concentration in solution. Because the ionic strength of the solution is kept constant, so the activity coefficient of hydrogen ion is constant too. The non-ideality of solutions is then included in E'_a (the specific constant of the potentiometric cell in the acidic region), so

$$E_{cell} = E'_a + k\log [H^+] \quad (2)$$

where E'_a is $E°_{cell} + k\log \gamma_{H+} + E_{LJ}$. The use of a glass electrode (with an aqueous inner solution) in non-aqueous media introduces a deviation from ideality. But it has been shown the deviation is negligible and the glass electrode is always usable in such media to measure H^+ concentrations with a linear relation of E_{cell} versus log $[H^+]$ [10].

In the acidic region the hydrogen ion concentration can be expressed as:

$$[H^+] = (M_{HClO4}V_0 - M_{NaOH}V_1) / (V_0 + V_1) \quad (3)$$

where M_{HClO4} and M_{NaOH} are the molarities of perchloric acid and sodium hydroxide, V_0 and V_1 are the initial volume of perchloric acid and the added volume of sodium hydroxide solution, respectively. In basic solution, the measured potential of the cell can be written as

$$E_{cell}\ (m\text{V}) = E°_{cell} + k\log a_{ClO4-} - k\log [OH^-] - k\log \gamma_{OH-} + E_{LJ} \quad (4)$$

so

$$E_{cell} = E'_b - k\log [OH^-] \quad (5)$$

where E'_b (the specific constant of the potentiometric cell in the basic region) is $E°_{cell} + k\log a_{ClO4-} - k\log \gamma_{OH-} + E_{LJ}$, a_{OH-} and γ_{OH-} are the activity and the activity coefficient of the hydroxyl ion, respectively. E'_b can be calculated from the intercept of the linear plot of E_{cell} versus – log $[OH^-]$. In the basic region hydroxyl ion concentration is expressed as:

$$[OH^-] = (M_{NaOH}V_1 - M_{HClO4}V_0) / (V_0 + V_1) \quad (6)$$

The autoprotolysis constant of water is then calculated from Eq. (7) and are listed in Table 1 for different aqueous methanol solutions together with the values reported in the literature for comparison [11].

$$pK_{ap} = (E'_a - E'_b) / k \quad (7)$$

Table 1. Average values of pK_{ap} of different aqueous solutions of methanol at 25 °C and ionic strength of 0.1 mol dm^{-3} ($NaClO_4$)

Methanol % (*v*/*v*)	pK_{ap}	Ref.
0	13.71 ± 0.08	This work
10	13.75 ± 0.07	″
15	13.81 ± 0.06	″
20	13.86 ± 0.09	″
25	13.90 ± 0.08	″
30	13.93 ± 0.07	″
35	14.00 ± 0.09	″
40	14.07 ± 0.07	″
45	14.12 ± 0.09	″
0	13.69	11
10	13.75	″
20	13.73	″
30	13.70	″
40	13.73	″

There are some differences between the autoprotolysis constants determined in this work and those were reported in the literature especially when the percentage of methanol is enriched in the mixed solvents. The main differences are due to the purity of the organic solvent used and some to the experimental method and that a background electrolyte has been used.

RESULTS AND DISCUSSIONS

Protonation of Histidine

The following species of the ligand may exist in solution at different pH, L^-, HL, H_2L^+, and H_3L^{2+}, where L^- represents the fully dissociated ligand anion. From Eq. (8), the protonation constants of histidine (K_1, K_2, and K_3) corresponding to n = 1, 2, or 3 refer to protonation of the amino, the charged amino of imidazole ring, and carboxylic acid groups of the ligand, respectively.

$$H_{n-1}L^{n-2} + H^+ \rightleftarrows H_nL^{n-1} \quad (8)$$

The protonation constant values of histidine were determined potentiometrically by titration of appropriate solutions of the ligand in different water-methanol mixtures. In this way, histidine was fully protonated at the beginning of a titration by adding a certain amount of perchloric 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/$HClO_4$-$NaClO_4$, H_3L^{2+} + H_2L^+ + HL + L^- in water-methanol/NaCl-$NaClO_4$/Ag-AgCl.

The fraction of protons still bound to the amino acid, $\bar{n}$, can be written as [12]:

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

where C_H and C_L are the total concentrations of protons and histidine, respectively. Substituting C_L and C_H in Eq. (9), leads to

$$n_{cal} = (K_1[H^+] + 2K_1K_2[H^+]^2 + 3K_1K_2K_3[H^+]^3) / (1 + K_1[H^+] + K_1K_2[H^+]^2 K_1K_2K_3[H^+]^3) \quad (10)$$

On the other hand, during a titration, electrical neutrality demands that the concentration of the cations should equal the concentration of the anions at all times, and hence, substituting $[L^-]$ from C_L in Eq. (9) and simplification leads to

$$n_{exp} = (C_L + [ClO_4^-] - [Na^+] - [H^+] + [OH^-]) / C_L \quad (11)$$

In Eqs. (10) and (11), $[Na^+]$ originates from the titrant used, $[ClO_4^-]$ is introduced from the perchloric acid added, $[H^+] = 10^{(Ecell - E'a) / k}$ and $[OH^-] = K_{ap}/[H^+]$. Using a suitable computer program (Microsoft Excel Solver) [13] the data from Eqs. (10) and (11) were fitted for estimating the protonation constant values of histidine in different aqueous solutions of methanol. We used the Gauss-Newton non-linear least-squares method in the computer program to refine the $\bar{n}$ values by minimizing the error square sum from Eq. (12).

$$U = \sum(\bar{n}_{exp} - \bar{n}_{cal})^2 \quad (12)$$

where $\bar{n}_{exp}$ is the experimental $\bar{n}$ and $\bar{n}_{cal}$ is the calculated one. The calculated protonation constant values of histidine in different water-methanol mixtures are listed in Table 2 together with the values reported in the literature for comparison [14-15]. With some differences, the protonation constant values obtained in this work are in agreement with those reported before. The main differences are due to the different experimental method and the fact that a different background electrolyte has been employed to determine the values.

Complexation of Mo(VI) with Histidine

The occurrence of molybdenum polymerization in acidic media complicates the study of molybdenum

complexation with the ligands [16]. Due to fact that the stability constants of the polymerization equilibria are not well-known, the region 5 < pH < 7 is useful for spectrophotometric determination. Using the continuous variations method, we determined the absorbances of solutions of Mo(VI) and histidine system with total concentration of 2.0×10^{-3} mol·dm^{-3} in the UV range (260-280 nm) at constant pC_H 5.8. The observed absorbances were corrected for unreacted Mo(VI) from Eq. (13) and are plotted in Fig. 1.

$$A_C = A_{obs} - \varepsilon_{Mo}[Mo(VI)] \quad (13)$$

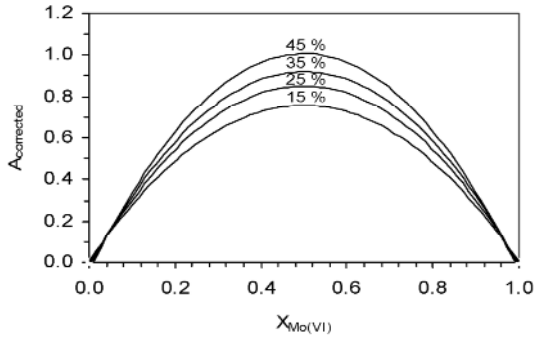

Fig. 1. Continuous variations plots of corrected absorbances of MoO_3L^- in different aqueous solutions of methanol at 25 °C, ionic strength 0.1 mol dm^{-3} ($NaClO_4$), and 275 nm.

Raymond et al [17] synthesized $Na(MoO_3L)H_2O$, among other molybdenum chelate complexes. The IR spectrum of those compounds that were crystallized at pH = 6 show that the tridentate ligands coordinated to a *cis*-trioxo molybdenum core. As well, Cruywagen [18] has demonstrated the acid dissociation of molybdic acid as

$$MoO_4^{2-} + 2H^+ \rightleftarrows H_2MoO_4 \quad (14)$$

Assuming that H_2MoO_4 is equivalent to MoO_3+H_2O, we can write the molybdenum(VI) chelate formation as Eq. (15). The same conclusion has been obtained before by Lagrange and her co-workers [19]. So, the composition of the complex species indicated by the spectrophotometric measurements at pC_H 5.8 is MoO_3L^-. The formation of 1:1 complex with the amino acid thus has Mo:ligand:proton equal to 1:1:2 stoichiometry as

$$MoO_4^{2-} + L^- + 2H^+ \rightleftarrows MoO_3L^- + H_2O \quad (15)$$

with the stability constant, K_S, as

$$K_S = [MoO_3L^-] / [MoO_4^{2-}][L^-][H^+]^2 \quad (16)$$

Thus, equations can be written for the total concentration of Mo, C_M, and total concentration of the ligand, C_L, at the maximum point on the plot, as described before [20-21].

$$C_M = [Mo(VI)] + [C] \quad (17)$$
$$C_L + [L^-] + [C] \quad (18)$$

where C is the complex species. Combining Eqs. (13), (17), and (18) in Eq. (16) and solving for K_S gives the stability constant of Eq. (15), which their average values at different wavelengths and various media are shown in Table 3 together with some homologous values reported before [22-23].

With some differences, the stability constant value of Mo(VI)-histidine resulting in this work is in agreement with those reported before. The main differences are due to the different ligands and the different experimental method.

SOLVENT EFFECT

Protonation Constant of Histidine

The three protonation constants of histidine in water-methanol mixed solvents have different behavior (Table 2). The protonation constant of the carboxylic acid, K_3, and the imidazole ring, K_2, groups of the ligand increased as the solvent became

enriched in the organic component, but the protonation constant of the amino group, K_1, decreased as methanol increased in the mixtures. It is very difficult to interpret the variation of the protonation constant values of histidine with respect to the percentage of methanol 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 [24-25] and a non-electrostatic term, which includes specific solute-solvent interactions. When the electrostatic effects predominate, then in accordance with the Born equation, Eq. (19), a plot of log K versus the reciprocal of the dielectric constant of the media, ε, should be linear.

$$\Delta \log K = (121.6z/r)(1/\varepsilon - 0.0128) \qquad (19)$$

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 $L^- \rightleftarrows HL$, $z = 0$ for the charge type $HL \rightleftarrows H_2L^+$ and $z = 2$ for the charge type $H_2L^+ \rightleftarrows H_3L^{2+}$.

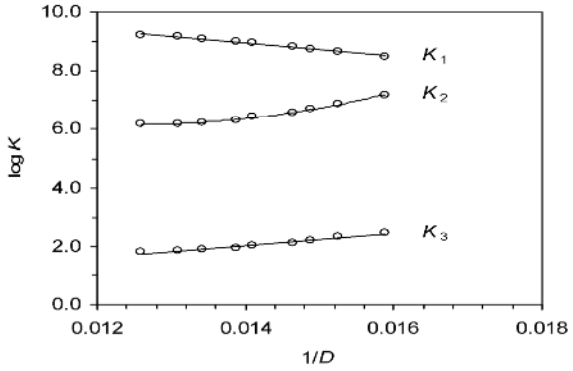

Fig. 2. Plots of the experimental values of log K_1, K_2, and K_3 versus the reciprocal of the dielectric constant of different mixed solvents at 25 °C and ionic strength 0.1 mol dm^{-3} ($NaClO_4$).

The correlation between log K_1 and log K_3 with the reciprocal of the dielectric constant of methanol-water mixtures are linear, with correlation coefficients 0.96 and 0.97, respectively (Fig. 2). However, there is no change in the number of charges involved in the protonation equilibria of the zwitterionic form of histidine, K_2. In this case, the correlation between log K_2 values and $1/\varepsilon$ is poor (Fig. 2) and so the protonation possibly depends on the solute-solvent interaction of the different species in the mixtures. Therefore, it is essential to elucidate the nature of solute-solvent interactions for a better understanding of solvent effects.

log K_2 values of histidine show small changes in the range 0 % to about 15 % (v/v) of methanol and a larger increase when the mixture is richer in methanol. 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 [25]. In fact, the water structure remains intact in the water rich region and the methanol molecules occupy the cavities between water molecules without changing the water structure [25]. In this region there are small changes in the log K_2 values of histidine. However, the log K_2 values change by larger amounts when the percentage of methanol increases to higher values. In this region the influence of methanol on water structure is high and the solute-solvent interactions cause a greater variation in 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 [24-27].

To obtain a quantitative method for evaluation of the solute-solvent interaction on protonation or the stability constants, we used the method introduced by Kamlet, Abboud and Taft (KAT) [28-29]. 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 [2]. The multiparametric equation, Eq. (20), has been proposed, using the solvatochromic solvent parameters, α, β and π^* which have been introduced in previous reports [22, 30].

$$\log K = A_0 + a\alpha + b\beta + p\pi^* \qquad (20)$$

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 hexamethylphosphoric 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) [13]. 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. (21).

$$U = \sum(\log K_{exp} - \log K_{cal})^2 \qquad (21)$$

The procedure used in the regression analysis involves a rigorous statistical treatment to find out which parameter in eq 20 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 20, was used as single, dual 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-methanol 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 [31-32], those are listed in Table 4. The expressions of the

KAT equation thus obtained for each property and are given as follows:

$$\log K_2 = 11.53(\pm 0.73) - 4.49(\pm 0.65)\alpha \quad (22a)$$

$N = 9$, $r^2 = 0.87$, ose = 0.13

$$\log K_2 = 2.27(\pm 0.53) + 7.64(\pm 0.96)\beta \quad (22b)$$

$N = 9$, $r^2 = 0.90$, ose = 0.12

$$\log K_2 = 15.40(\pm 0.76) - 8.18(\pm 0.70)\pi^* \quad (22c)$$

$N = 9$, $r^2 = 0.95$, ose = 0.08

Although the solvent polarity is identified as the main reason of the variation of log K values in water-methanol mixtures, but the results show any single-parameter correlations of log K_1, log K_2, and log K_3 values individually with π^*, α, and β did not give good results in all cases. However, the correlation analysis of log K_1, log K_2, and log K_3 values with dual-parameter equations (including α and π^*) indicate significant improvement with regard to the single and multi-parameter models. To indicate the importance of the KAT parameters, the uncertainty values for each term in Eqs. (22) and (23) are shown in the bracket using Linest program.

$$\log K_3 = 8.714(\pm 0.60) + 1.16(\pm 0.74)\alpha - 7.31(\pm 1.29)\pi^* \quad (23a)$$

$N = 9$, $r^2 = 0.99$, ose = 2.50×10^{-2}

$$\log K_2 = 19.16(\pm 1.30) + 5.01(\pm 1.60)\alpha - 16.79(\pm 2.79)\pi^* \quad (23b)$$

$N = 9$, $r^2 = 0.98$, ose = 5.42×10^{-2}

$$\log K_1 = 1.34(\pm 0.46) - 1.42(\pm 0.57)\alpha + 8.44(\pm 0.99)\pi^* \quad (23c)$$

$N = 9$, $r^2 = 1.00$, ose = 1.93×10^{-2}

The coefficients of α and π^* in Eqs. (23a) to (23c) are different from each other and are in the order of $\pi^* > \alpha$ in protonation of the amino acid. This indicates the polarity parameter plays a major role in all cases, but the hydrogen-bond donor acidity parameter of the solvent has less significance in the correlation analysis in the variation of protonation constant values of histidine in the proposed various aqueous solutions of methanol.

If the dielectric constant of the media was the only factor for the solvent effect on the 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 methanol. It can be seen from Table 4 that the dielectric constants of the solvent mixtures decrease as the solutions are enriched in methanol. The values of log K_3 and log K_2 increase with decreasing 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 negative π^* coefficients in the correlation analysis of log K_3 and log K_2 by the KAT equation imply that a decrease in the polarity of the mixed solvents, increases the protonation constant values of the amino and the charged amino of the imidazole ring groups of histidine. According to this discussion, the positive π^* coefficient obtained for log K_1 represents a decrease in polarity of the solvent mixtures causes a decrease in the protonation constant values of the amino group. This indicates the polarity parameter, π^*, is the most important (with a relatively large difference with the other coefficients) in the correlation analysis of the protonation constants of histidine. In a previous work, in correlation analysis of the protonation constants of cysteine and penicillamine in

aqueous solutions of methanol, almost the same results were obtained [4, 30]. Furthermore, the positive coefficient α in the correlation of log K_3 and log K_2 and negative in the case of log K_1 suggests that the increasing basicity of the solvent mixtures increases the protonation constant of the carboxylic and imidazol ring groups of histidine and decreases the protonation constants of the amino group of the compound. This could be due to the charges involved in the protonation equilibria. An increase in the basicity of the mixtures increases the solvation of the cationic species of the amino acid, and therefore makes protonation equilibrium more likely. However, this is not true in the case of K_1 that have a negative coefficient of α.

Table 2. Average values of experimental protonation constants: carboxylic acid, K_3, charged amino of imidazole ring, K_2, amino, K_1, groups of L-histidine at 25 °C, different aqueous solutions of methanol, and ionic strength of 0.1 mol dm^{-3} ($NaClO_4$)

Methanol % (v/v)	log K_3	log K_2	log K_1	Ref.
0	1.81	6.18	9.21	This work
10	1.86	6.20	9.17	″
15	1.91	6.24	9.11	″
20	1.95	6.31	9.02	″
25	2.03	6.44	8.96	″
30	2.14	6.58	8.85	″
35	2.21	6.71	8.75	″
40	2.33	6.87	8.65	″
45	2.45	7.19	8.48	″
0	-	6.05	9.16	14
0	1.79	6.00	9.16	15

Complexation Constant

In order to explain the obtained log K_S values through the KAT equation, the formation constants were correlated with the solvent properties by means of single, dual, and multiple linear regression analysis using the same computer program (Microsoft Excel Solver and Linest). We again used the Gauss-Newton non-linear least-squares method in the computer program to refine the log K_S by minimizing the error squares sum from eq 21. Single-parameter correlations of log K_S individually with α, β, or π^* again did not give a good result. However, the result presented in Eq. (24), dual-parametric equation, indicates significant improvement with regard to the single and multi-parameter models.

$$\log K_S = 22.96(\pm 0.86) + 2.47(\pm 0.51)\beta - 5.09(\pm 0.54)\pi^* \quad (24)$$

$N = 9$, $r^2 = 1.00$, ose = 9.51×10^{-3}

In this case the solvent polarity parameter of the media, π^*, has again a major role. If the π^* of the media was the only factor for describing the solvent effect on complexation, it may be expected that the log K_S in water should be greater than those of all the other aqueous solutions of methanol. However, the formation constant of the complex species increase with an increase in the solvent hydrogen-bond acceptor basicity parameter, β, and decrease with increasing solvent polarity π^*. The coefficients of π^* and β in Eq. (23) are in the order of $\pi^* > \beta$. This suggests that the polarity parameter power of the solvent is the most important and the hydrogen-bond acceptor basicity parameter plays a relatively small role in changing the formation constants of the Mo(VI) + histidine

Table 3. Average values of the experimental stability constants of Mo(VI)-histidine system at 25 °C, pC_H 5.8, different aqueous solutions of methanol, and ionic strength 0.1 mol dm^{-3} ($NaClO_4$)

Methanol % (*v/v*)	log K_S	Ref.
0	18.37 ± 0.05	This work
10	18.46 ± 0.05	″
15	18.57 ± 0.03	″
20	18.68 ± 0.06	″
25	18.78 ± 0.08	″
30	18.92 ± 0.04	″
35	19.03 ± 0.03	″
40	19.15 ± 0.05	″
45	19.29 ± 0.09	″
0	18.37	7
0 Mo(VI)-aspartic acid	18.70	22
0 Mo(VI)-glutamic acid	17.54	22
0 Mo(VI)-nitrilotriacetic acid	17.85	23

Table 4. KAT solvatochromic parameters and the dielectric constants of different methanol-water solvent mixtures

Methanol % (v/v)	α	β	π^*	ε
0	1.23	0.49	1.14	79.50
10	1.19	0.51	1.13	76.40
15	1.17	0.53	1.12	74.49
20	1.14	0.54	1.10	72.10
25	1.11	0.56	1.09	70.98
30	1.08	0.57	1.07	68.13
35	1.06	0.59	1.06	67.15
40	1.04	0.60	1.04	65.16
45	1.02	0.62	1.02	6300

Table 5. Percentage contribution of KAT parameters on the effect of different media on protonation and complexation at 25 °C and ionic strength 0.1 mol dm^{-3} ($NaClO_4$)

species	α	β	π^*
log K_1	14.4	-	85.6
log K_2	23.0	-	77.0
log K_3	13.7	-	86.3
log K_S	-	32.7	67.3

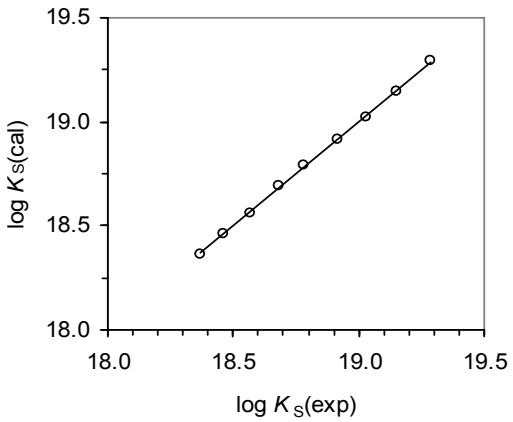

Fig. 3. Plot of the experimental values of log K_S versus the calculated ones at 25 °C and ionic strength 0.1 mol dm^{-3} ($NaClO_4$).

CONCLUSIONS

The protonation of histidine and its complexation by molybdenum(VI) have been determined in different aqueous solutions of methanol. The log *K* values obtained in the water-methanol mixtures were correlated with the solvation parameters of the solvents including the dielectric constants and the KAT parameters. Although the solvent polarity is identified as the main reason for the variation of the formation constants in water-methanol mixtures, excellent linear relationships were obtained with the dual parameter equations that include α and π^* (in protonation) and β and π^* (in complexation) processes. The obtained results show that the dielectric constant as a single parameter cannot serve as a quantitative measurement of solvent polarity for such studies.

REFERENCES

[1]. W. Nernst, *Z. Phys. Chem*. 13 (1984) 531.

[2]. C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry*, 3nd Ed., VCH, New York, (2004).

[3]. Z. Staszak, A. Bartecki, *Spectr. Lett*. 22 (1989) 1193.

[4]. F. Gharib, *J. Chem. Eng. Data* 55 (2010) 1547.

[5]. A. Shamel, F. Jaberi, F. Gharib, *J. Chem. Eng. Data* 55 (2010) 5176.

[6]. F. Gharib, M. Malekani, *Rev. Inorg. Chem*. 23 (2003) 97.

[7]. A.E. Fazary, A. F. Mohamed, N. S. Lebedeva, *J. Chem. Thermodynamics* 38 (2006) 1467.

[8]. L. Pehrsson, F. Ingman, A. Johansson, *Talanta* 23 (1976) 769.

[9]. P. Gameiro, S. Reis, J. L. F. C.Lima, B. de Castro, *Anal. Chim. Acta* 405 (2000) 167.

[10]. J. S. Jaime Ferrer, E. Couallier, M. Rakib, G. Durand, *Electrochim. Acta* 52 (2007) 5773.

[11]. E. Kilic, N. Aslan, *Microchim. Acta* 151 (2005) 89.

[12]. M. T. Beck, I. Nagypal, *Chemistry of Complex Equilibria*, Ellis Harwood, New York, (1990).

[13]. N. Maleki, B. Haghighi, A. Safavi, *Micochem. J*. 62 (1999) 229.

[14]. I. D. Chawla, A. C. Andrews, *J. Inorg. Nucl. Chem*. 32 (1970) 91.

[15]. W. E. VanDer Linden, C. Beers, *Anal. Chim*. 68 (1973) 143.

[16]. E. S. Johansen, O. Jons, *Acta Chem. Scand*. 35 (1981) 233.

[17]. J. Raymond, H. Butcher, J. Kipton, J. Powell, *J. Chem. Soc. Dalton Trans*. (1976) 356.

[18]. J. J. Cruywagen, B. B. Heyns, E. A. Rohwer, *J. Chem. Soc. Dalton Trans*. (1993) 1713.

[19]. K. Zare, P. Lagrange, J. Lagrange, *J. Chem. Soc. Dalton Trans*. (1979) 1372.

[20]. F. Gharib, K. Zare, K. Majlesi, *J. Chem. Eng. Data* 45 (2000) 833.

[21]. F. Gharib, K. Zare, A. Taghvamanesh, M. Monajjemi, *J. Chem. Eng. Data* 46 (2001) 1140.

[22]. F. Gharib, M. Jabbari, A. Farajtabar, A. Shamel, *J. Chem. Eng. Data* 53 (2008) 1772.

[23]. F. Gharib, K. Zare, B. Mohammadi, *J. Mol. Liq*. 124 (2006) 63.

[24]. J. Barbosa, D. Barron, J. L. Beltran, S. Buti, *Talanta* 45 (1998) 817.

[25]. J. Barbosa, I. Toro, V. Sanz-Nebot, *Anal. Chim. Acta* 347 (1997) 295.

[26]. H. Demirelli, *J. Sol. Chem*. 34 (1991) 1283.

[27]. Y. Marcus, Y. Migron, *J. Phys. Chem*. 95 (1991) 400.

[28]. R. W. Taft, J. L. M. Abboud, M. J.

Kamlet, *J. Org. Chem*. 49 (1984) 2001.
[29]. M. J. Kamlet, J. L. M. Abboud, M. H. Abraham, R. W. Taft, *J. Org. Chem*. 48 (1983) 2877.
[30]. F. Gharib, A. Shamel, *J. Chem. Eng. Data* 54 (2009) 933.
[31]. U. Buhvestov, F. Rived, C. Rafols, E. Bosch, M. Roses, *J. Phys. Org. Chem*. 11 (1998) 185.
[32]. S. M. Puranik, A. C. Kumbharkhane, S. C. Mehrota, *J. Mol. Liq*. 59 (1994) 173.