Potentiometric Determination of Dissociation Constants and Gibb's Free Energies of 8-Hydroxyquinoline (oxine) and 2-Methylquinoline Using Aqueous and Mixed Organic-water Solvent Systems

H. A. B. INDHAR AND A.W.K. KHANZADA*

Centre of Excellence in Analytical Chemistry
University of Sindh, Allama I. I. Kazi Campus,
Jamshoro, Sindh, Pakistan

Summary: The dissociation constants (pK$_a$'s) and thermodynamic parameters Gibb's free energies (ΔG) have been determined by a potentiometric pH titration of 8-hydroxyquinoline (oxine) in water at 25 to 50°C and for 2-methylquinoline in water and in aqueous binary mixtures of dioxane, ethanol (EtOH) and methanol (MeOH) at 25°C ± 0.1°C.

The first and second dissociation constants of oxine have been analyzed and discussed with (ΔG) thermodynamic parameters. The pK values and thermodynamic parameters of 2-methylquinoline have also been computed and discussed in term of solute-solvent interactions. The curves found in both the compounds are a part of a parabola and these follow quadratic equations.

The results are correlated with dielectric constant of medium and discussed in terms of solvent characteristics, solvent basicity and stabilization of conjugate acid for base by hydrogen bonding interaction in hydro-organic solvent media.

Introduction

The ionization constant is an important parameter in determining the behaviour of compounds in various applications. It is used to measure the strength of acids and bases. The dissociation constants (pK$_a$) of weak acids and bases are widely used in pharmaceutical industries, in spectroscopy and in biological sciences. The pK$_a$'s are useful criteria of identifying particularly the substances which do not melt [1-3]. The term ionization constant is referred to dissociation constant which is a vague expression, not necessarily connected with ionization [4]. Among the physico-chemical properties of molecules, the ionization constants are of vital importance, both in analysis of drugs as well as in the in the interpretation of their mechanism of action [5].

The aim of the present study is:

(i) to find out the pK$_a$ values and thermodynamic parameters of 8-hydroxyquinoline in

*To whom all correspondence should be addressed.

aqueous medium and to analyze the effect of temperature on acid base equilibria of the compound from 20 to 50°C.

(ii) To deal with influence of solvents on acid base equilibria and to obtain a solvent independent acidity or basicity scale and to extend the study of 2-methylquinoline base strength in different co-solvent systems such as dioxane-water, EtOH-water and MeOH-water at 25°C. The percentage composition of organic components is varied from 10% to 50% in the step of 5% each. The methyl derivatives are generally not soluble in water [6]. Dissociation constants have been reported in mixed solvent systems e.g., in chloroform [4]. The most important advantage of non-aqueous medium usually an organic solvent is that a large number of substances that are insoluble in water are readily soluble in non-aqueous solvents. Another advantage of the use of non-aqueous medium is that a large variety of solvents are available and they have differing acid base properties [7].

There are different methods [3,7-10] that are being used for the determination of dissociation constants of weak bases and acids. These methods have certain limitations, such as solubility, range of pK$_a$ and time requirements etc. [8-11]. The best and quick method for this purpose is potentiometry [3,7-13], while spectrophotometry is very accurate but it is time consuming [8-11]. These pK$_a$ values are obtained by analyzing the experimental data with a computer program written in GW-BASIC to work on IBM PC [14].

The potentiometry is well known instrumental method in which the potential of an indicator electrode is measured. The potential of this electrode is reversible towards the concentration of certain ions. It draws small current from the cell, i.e., it measures the potential when the cell reaction is proceeding simultaneously at a small rate. The device designed for reversible [15-16] measurement is known as potentiometer. The most commonly used electrode system for potentiometric titration is a glass electrode in combination with a saturated silver-silver chloride used as reference electrode.

The 8-hydroxyquinoline (oxine) forms chelated complex with a large number of metals and displays both acidic and basic properties and it is an amphoteric substance [4]. The term amphoteric is mostly applied to the oxides and hydroxides of metals that can form both cations and complex anions. For example, zinc oxide dissolves in acids to form zinc salts and also it dissolves in alkalies to form zincates [17].

Theory

Theory of dissociation is well-documented [18-19]. The ionization constant for an acid HA is:

$$pK_a^M = pH + \log \frac{[HA]}{[A^-]} \qquad (1)$$

and for a base BH$^+$ it is:

$$pK_b^M = pH + \log \frac{[BH^+]}{[B]} \qquad (2)$$

Where the term in square brackets [ ] indicate molar concentrations. The respective thermodynamic equations for dissociation constants K$_a^T$ are:

$$\text{for acid } K_a^T = \frac{a_{H^+} \cdot a_{A^-}}{a_{HA}} \qquad (3)$$

$$\text{and for a base } K_a^T = \frac{a_{H^+} \cdot a_B}{a_{BH^+}} \qquad (4)$$

Where a$_A$ =[A$^-$]γ_{A^-} etc. Here a is an activity and γ is activity coefficient of respective ionic specie. Activity coefficient γ_i of ion i is given by Debye-Hückel theory [3]

$$- \log \gamma_i = \frac{Az^2 \sqrt{I}}{1 + Ba_i \sqrt{I}} \qquad (5)$$

$$pK_a^T = pK_a^M \pm \frac{0.507 \ I^{1/2}}{1 + 1.5 \ I^{1/2}} \qquad (6)$$

where (+) sign is for an acid and (-) sign is for a base [3]. In eq. (5) and eq. (6), I is the ionic strength [3] defined by:

$$I = \frac{1}{2} \Sigma C_i \ z_i^2 \qquad (9)$$

where C$_i$ and z$_i$ are molar concentration and charge of ion i respectively.

Results and Discussions

(i) 8-Hydroxyquinoline (Oxine)

In 8-hydroxyquinoline or oxine there are two substituent groups: one is basic and other is acidic. Having two ionizing groups, two dissociation constants are possible: one for proton gained and the other for proton lost. Amphoteric compounds can be titrated with an acid to yield the basic group pK_a^M (concentration ionization constant) and with an alkali to yield the pK_b^M (concentration ionization constant) of the acidic group [19].

The results show the effect of temperature on pK_a^M, pK_a^T, pK_b^M and pK_b^T values of 8-hydroxyquinoline. It is noted that by increasing the temperature both dissociation constant values decrease. Ionization constant shows similar trend as the 8- substituted derivatives (8-methyl and 8-aminoquinoline) have shown [20-21]. The pK_a^M values in basic mode decrease with temperature in a similar way as those of quinoline except the magnitude of pK_a value is slightly higher than that of quinoline [22]. At 20°C in basic mode (proton gained), pK_a^M is 5.122 ± 0.004 as the temperature increases to 50°C, the pK_a^M value drops up to 4.443 ± 0.006 .

The ionization constants vary with the temperature. The correlation curve is usually a parabola with a flat maximum. A change in temperature causes a shift in equilibrium point, which

is both of practical and theoretical interest. Nitrogenous bases [3] are highly temperature sensitive, become weaker as temperature is increased. Temperature effect is much greater with the stronger bases compared to weaker ones. The organic bases have over all much greater temperature coefficient than organic acids.

In acidic mode (proton lost) pK_b^M value of oxine is higher and decreasess with the increase of temperature. The data given is Table 1 and Table 2 further clarify the effect of temperature on pK_a^M, pK_a^T, pK_b^M and pK_b^T for 8-hydroxyquinoline. The thermodynamic parameter viz. Gibb's free energies ΔG associated with proton dissociation constants were calculated utilizing the standard equations.

$$\Delta G = -RT\ln K = RT\ln(10)pK \qquad (7)$$

The Gibb's free energies are calculated from the values of both pK_a^M, pK_a^T, pK_b^M and pK_b^T from 20 to 50°C. Table 1 and Table 2 show that an increase in temperature causes a decrease in the ΔG values and the curve of ΔG versus temperature when drawn is a parabola (quadratic equation). The graph of pK versus temperature (x) and related ΔG versus temperature follow generally a quadratic equations. These equations are given in Table 3 and are obtained by polynomial regression of second degree. Their coefficient of determination R^2 are also given.

The high proportion of dipolar ion in aqueous solution of oxine is due to inductive effective of two

Table 1: Effect of Temperature on pK_a^M, pK_a^T and Thermodynamic Constants of 8-Hydroxyquinoline in Aqueous Solution (Proton gained)

S.No.	Temp: In °C	pK_a^M	pK_a^T	ΔG of pK_a^M kcal/mol	ΔG of pK_a^T kcal/mol
1	20	5.122 ±0.004	5.087±0.011	6.869± 0.006	6.822± 0.015
2	25	4.992±0.005	4.956 ± 0.013	6.809± 0.007	6.761± 0.017
3	30	4.817 ± 0.005	4.781 ± 0.011	6.682± 0.007	6.632± 0.015
4	35	4.634 ± 0.005	4.598 ± 0.009	6.534± 0.007	6.483± 0.012
5	40	4.556 ± 0.005	4.519± 0.012	6.528± 0.007	6.475± 0.017
6	45	4.507 ± 0.004	4.470± 0.009	6.560± 0.005	6.507± 0.012
7	50	4.443± 0.006	4.405± 0.011	6.568± 0.008	6.513± 0.017

Table 2: Effect of Temperature on pK_b^M and pK_b^T and Thermodynamic Constants of 8-Hydroxyquinoline in Aqueous Solution (Proton lost)

S.No.	Temp in °C	pK_b^M	pK_b^T	ΔG of pK_b^M Kcal/mol	ΔG of pK_b^T Kcal/mol
1	20	9.889 ±0.003	9.916±0.006	13.263± 0.005	13.299± 0.009
2	25	9.812± 0.002	9.839± 0.005	13.385± 0.003	13.421± 0.007
3	30	9.724± 0.004	9.751± 0.005	13.487± 0.006	13.525± 0.007
4	35	9.633± 0.002	9.660± 0.005	13.581± 0.002	13.620± 0.008
5	40	9.542± 0.004	9.569± 0.005	13.671± 0.005	13.711± 0.007
6	45	9.408± 0.003	9.435± 0.005	13.694± 0.004	13.734± 0.008
7	50	9.272± 0.003	9.300± 0.006	13.709± 0.004	13.751± 0.009

Table 3: Equations obtained by polynomial regression between pK and ΔG versus temperature in oxine

(a)   In acidic mode

pK_a^M		ΔG of pK_a^M	
$y = 0.0006x^2 - 0.0623x + 6.1682$	$R^2 = 0.9912$	$y = 0.0007x^2 - 0.0584x + 7.7989,$	$R^2 = 0.9395$
pK_a^T		ΔG of pK_a^T	
$y = 0.0006x^2 \ 0.0624x + 6.1337,$	$R^2 = 0.9914$	$y = 0.0007x^2 \ 0.0588x + 7.7588,$	$R^2 = 0.9412$

(b)   In basic mode

pK_b^M		ΔG of pK_b^M	
$y = -0.0003 \ x^2 - 0.0028x + 10.04,$	$R^2 = 0.999$	$y = -0.0004x^2 + 0.0466x + 12.504,$	$R^2 = 0.9964$
pK_b^T		ΔG of pK_b^T	
$y = -0.0002x^2 - 0.0029x + 10.069,$	$R^2 = 0.999$	$y = -0.0004x^2 + 0.0468x + 12.536,$	$R^2 = 0.9964$

In above equations y = pK or ΔG and x = temperature in °C.

groups. The cation strengthens the acid group and the anion strengthens the basic group. This effect should therefore fall off with distance and be quite small in such substances as 8-hydroxyquinoline where pK_a^M value of 5.122 ± 0.004 may be taken as an acidic and pK_b^M value of 9.889 ± 0.003 taken as a basic value. The 8-hydroxyquinoline differs from other quinolinols in the stereo relationship of hydroxyl group to nitrogen, because of this, many metallic ions form insoluble chelate compounds with oxine hence it is one of the most valuable organic reagent for estimation of metallic ions.

(ii) 2-Methylquinoline

Methyl derivatives of quinoline are considerably dissociated in aqueous media. The pK values of of 2-methylquinoline are higher than those of quinoline [22]. It means this derivative dissociates slower than quinoline. The insertion of methyl group usually gives rise to the base strengthening effect (0.3 to 1.0 pK_a^M unit of quinoline). The protonation constants of 2-methyl-quinoline are determined in water at 20, 25, 30, 35, 40, 45 and 50°C and in percent composition from 10, 15, 20, 25, 30, 35, 40, 45 and 50 percent in organic-water solvent mixtures at 25°C.

The dissociation constant of 2-methyl-quinolines furnishes useful information for the interpretation of the properties of the substance [23]. The ionization constant varies with the temperature. The correlation curve usually follows a quadratic equation. Increase in temperature causes decrease in pK_n values. Fig. 1 further clarifies the effect of temperature on ionization constant pK_a and Gibb's free energy ΔG values in aqueous solution

The ionization constants and thermodynamic parameter ΔG for methyl derivatives in solution comprising aqueous mixtures are useful in
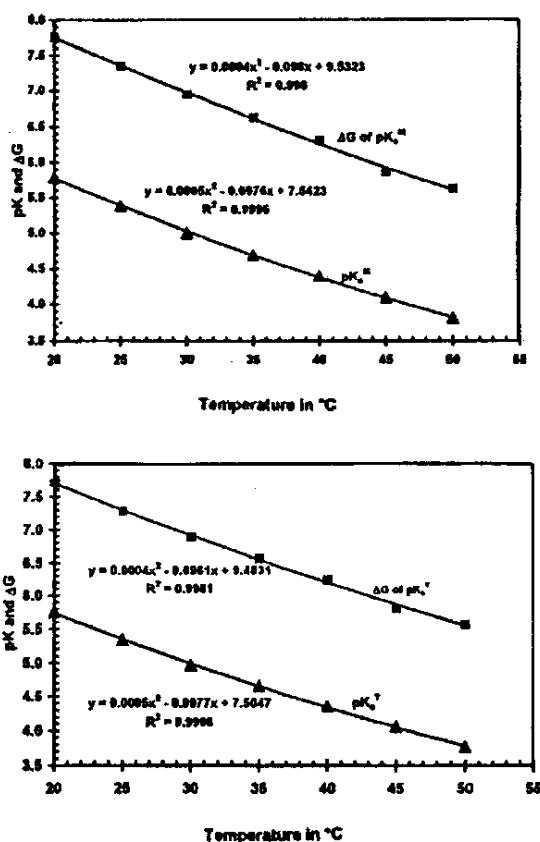

Fig. 1. Effect of temperature on pK_a, and ΔG of pK_a of 2-methylquanoline in aqueous solution. Top curves are for pK_a^M and ΔG of pK_a^M and bottom curves are for pK_a^T and ΔG of pK_a^T.

understanding the solvent effect. The ionization constants pK_a^M and pK_a^T of 2-methylquinoline decrease with the increase of percent composition in all the three solvent systems as shown in Fig. 2 to Fig. 4. These figures show that pK_a value in 50%

dioxane-water is 4.591 ± 0.003, in 50% EtOH, it is 5.212 ± 0.006 and in 50% MeOH-water system it is 5.088 ± 0.006. The effect is most pronounced because the hyperconjugative effect on the methyl group in these positions would be base strengthening. Methyl group in 6th and 8th position do not increase the availability of electrons on nitrogen atom and are not base strengthening [22-22, 24]. In monomethyl-quinoline series, the location of methyl radical on the nitrogen ring seems to have a larger influence upon ionization than does on benzene ring. The graph of pK_a versus percent composition is a parabola. ΔG values of 2-methylquinoline decreases with the increase of percent composition. We have calculated
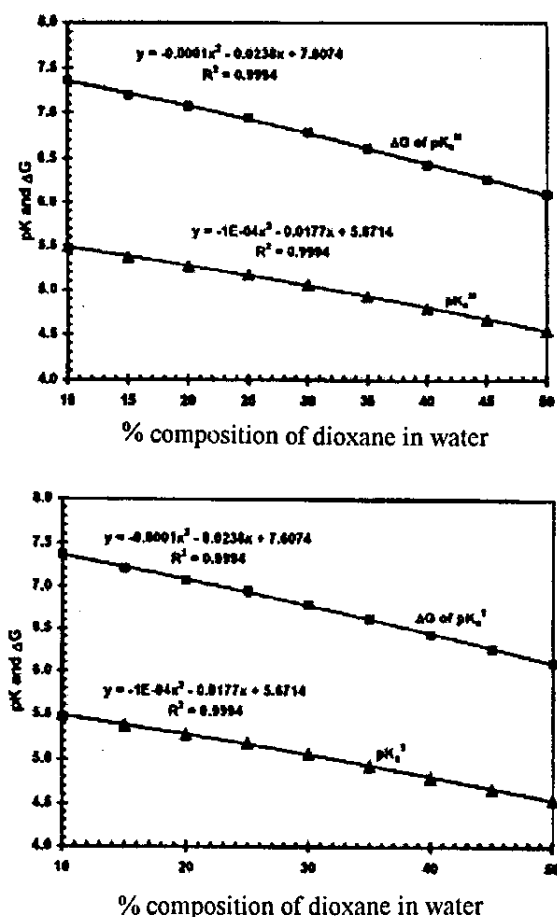
Gibb's free energies ΔG from the value of pK_a^M and pK_a^T in aqueous and in 10 to 50 percent solvent systems. It is observed that there is a regular decrease in Gibb's free energy (ΔG) with increase of temperature and percent composition of mixed organic-water solvents as shown in Fig 2 for dioxane in Fig. 3 for EtOH and in Fig. 4 for MeOH. Same pattern is observed for ΔG values of pK_a^T. As the temperature increases, the ΔG of pK_a^M and ΔG of pK_a^T decreases (Fig. 2 to Fig. 4).
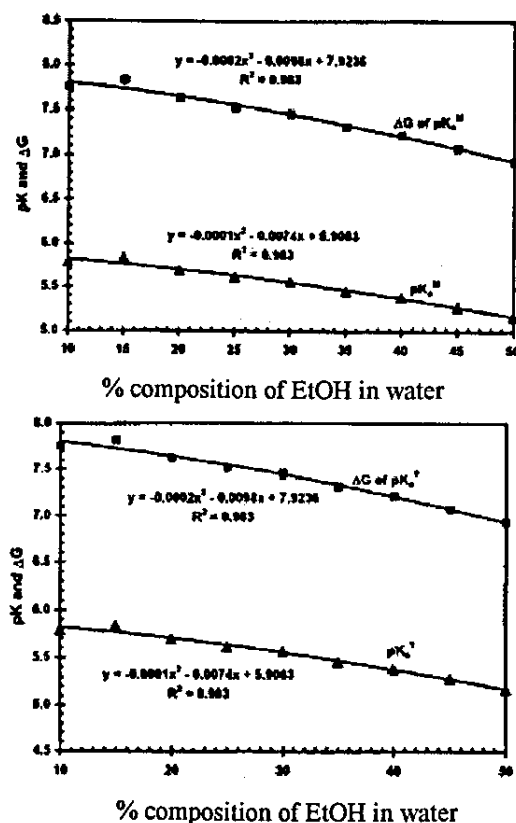

% composition of EtOH in water

% composition of EtOH in water

Fig. 3. Effect of percent EtOH composition in aqueous solution of 2-methylqinoline on as pK and ΔG. Top curves: (pK_A^M and ΔG of PK_a^M) Bottom curves: (pK_a^T and ΔG of pK_a^T)

% composition of dioxane in water

% composition of dioxane in water

Fig. 2. Effect of percent Dioxane composition in aqueous solution of 2-methylquinoline on pK and ΔG of 2-methylquinoline. Top (pK_a^M and ΔG of pK_a^M vesrus Percent Composition of Dioxane)Bottom (pK_a^T and ΔG of pK_a^T vesrus Percent Composition of Dioxane)

The degree of dissociation of the compound varies with percent composition of solvent-water system and temperature. Solvents are distinguished from their dielectric constants and hydrogen-bonding capabilities. Water, EtOH, and MeOH have greater hydrogen bonding capacity and dielectric constant of 78.5, 32.6 and 24.3 respectively. In pure water pK_a values are highest and MeOH-water has lowest values. Dioxàne has lowest dielectric constant of 2.21
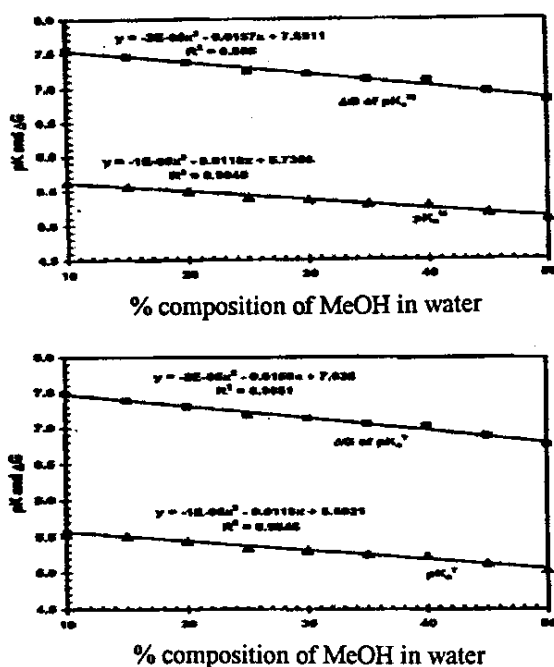
% composition of MeOH in water

% composition of MeOH in water

Fig. 4. Effect of percent MeOH composition in aqueous solution of 2-methylquinoline on its pK and related ΔG. Top: (PK_a^M and ΔG of pK_a^M) Bottom : (PK_a^T and ΔG of pK_a^T)

and no ability to form H-bond. The pKa values in this system are therefore lowest.

Experimental

Chemical Used

The following chemicals of analytical grade were obtained from Fluka and Merck. These were used without further purification. These were: Sodium hydroxide, hydrochloric acid, potassium chloride, potassium nitrate, potassium hydrogen phthalate, potassium di-hydrogen phosphate, di-sodium phosphate, 8-hydroxyquinoline and 2-methylquinoline.

Preparation of Solution

Carbon dioxide free standard sodium hydroxide solution of 1 M was prepared and it was further diluted to 0.01 M. The solution prepared for the compounds (8-hydroxyquinoline and 2-methylquinoline) analyzed is 0.01 M (in acidic and basic media). Through out the work double distilled and de-ionized water obtained through an ion-exchange column has been used. The conductivity is

sufficiently low i.e., $1x\ 10^{-6}\ Sm^{-1}$. Carbon dioxide free water was prepared by boiling double distilled water for 20 minutes in a round bottom flask and cooling it with absorption tower protection passing nitrogen gas through it. Ordinary nitrogen gas contains contamination of carbon dioxide and oxygen. The equilibrium chemists have recommended that there should not be more than 2 percent CO_2 in sodium hydroxide solution [3], for this purpose the solution of NaOH is standardized potentiometrically with primary standard potassium hydrogen phthalate, which was first dried at 120°C. Further the percentage of carbon dioxide in sodium hydroxide is calculated by the Gran's plot method [25]. From this method it is observed that 1.25 percent carbon dioxide was present which is under the level of recommendations. The buffer solutions of 0.05 M potassium hydrogen phthalate (pH=4.00 at 25°C), 0.025 M potassium di-hydrogen phosphate (pH 6.89 at 25°C) and 0.1 M sodium tetraborate (pH 9.18 at 25°C) were prepared in water [26].

Experimental Procedure

The Philips PW 9420, 3½ digit digital pH meter was used which was coupled with Ingold combined glass and Ag/AgCl reference electrode filled with 3 molar potassium chloride. The glass electrode was calibrated against the buffer solutions of different pH-scale [26]. All the measurements of sample solution were performed in double walled glass cell. At each step the temperature of the sample solution was maintained constant by circulating water through the jacketed measuring cell. JULABO HC thermostated bath accurate to ± 0.1°C is connected to Grant cool-nit for the required temperature control below 30°C. The sample was kept inert by bubbling and passing dried and pure nitrogen through out the course of titration [27]. The sample solution was kept mixed by stirring with magnetic stirrer. For dispensing titrant Mettler burette DV-10 accurate to 0.01 ml was used. Titrating 20 or 25 ml of sample solution in aqueous media performed all the potentiometric measurements.

Conclusions

(i) 8-Hydroxyquinoline

The oxine has two dissociation constants one for acidic (proton gained) and the other for basic (proton lost). The dissociation constant values of 8-hydroxyquinoline are higher than those of quinoline.

The dissociation constants pK_a and Gibb's free energy ΔG values decrease with temperature. The second dissociation constant $pK_b{}^M$ varies from 9.889 ± 0.003 at $20°C$ to 9.272 ± 0.003 at $50°C$. Gibb's free energy values of this $pK_b{}^M$ also decrease with the increase of temperature.

(ii) 2-Methylquinoline

The pK_a values of solvents other than water are different from those which are in aqueous solutions e.g. pK_a of 2-methylquinoline in water at 20 °C is 5.768 ± 0.005, in 50% dioxane is 4.591 ± 0.003, in 50% EtOH is 5.212 ± 0.006 and in 50% MeOH is 5.088 ± 0.006. It is observed that concentration ionization constant $pK_a{}^M$ and thermodynamic ionization constant $pK_a{}^T$ values in aqueous solutions decrease with rise of percent composition. The curve of pK_a verses percent composition is a parabolic one (follows a quadratic equation). In case of dioxane-water, EtOH-water and MeOH-water solvent systems $pK_a{}^M$ and $pK_a{}^T$ verses percent composition decrease slowly by increasing the addition of the solvents. The curve of the $pK_a{}^M$ and pKa^T verses percent composition follows a quadratic equation.

In case of thermodynamic functions there is regular decrease in ΔG of $pK_a{}^M$ and ΔG of $pK_a{}^T$ versus temperature and percent composition in all the three solvents. After going through the data it is concluded that temperature and solvent have significant effect on $pK_a{}^M$, $pK_a{}^T$, ΔG of $pK_a{}^M$ and ΔG of $pK_a{}^T$ values of 2-methylquinoline.

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