

# Dissociation Constant Studies of Citric Acid at Different Temperatures and in Different Organic-Water Solvent Systems

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**Summary:** Thermodynamic dissociation constants of citric acid is being studied at different temperatures from 25 to 50°C at 5°C interval and in 10, 20, 30 and 40 percent v/v dioxane-water, methanol-water, ethanol-water and acetonitrile-water solvent systems. The resolution of acid strength in dioxane, methanol, ethanol and acetonitrile relative to that in water has been determined. Thermodynamic parameters that are Gibb's free energy ( $\Delta G$ ), enthalpy ( $\Delta H$ ) and entropy ( $\Delta S$ ) at different temperature have also been studied. Changes in  $pK_a$  values on account of dielectric constant and hydrogen bonding have been discussed. Result shows greater resolution in mixed organic solvents than in water.

## Introduction

The purpose of this work was to extend the study of acid strength at different temperature and in different co-solvent systems. Because of ion-pair formation in different medium, the incomplete dissociation of the salt formed in the titration has been taken into account in computing the  $pK_a$  values.

Citric acid ( $H_3Ci$ ) is an essential component in all living beings. They directly takes part in the production of energy through the tricarboxylic acid cycle, as well as in several processes associated in the metabolism of fatty acids, carbohydrates and certain amino acids [1].

Citric acid is widespread within the plant kingdom and is often predominant in the total

carboxylic acid content. Therefore, it is a commonly used parameter in the analysis of plants and their derivatives. Further more, owing to its innocuity it is often used as an antibacterial substance and as an additive for the control of pH [2].

Citric acid has been used as a growth inhibitor in electrolytic deposition of various metals [3], as a buffer masking agent for various metal ions and as an eluting agent in ion-exchange chromatography [4-5]. Some of these applications are based on the ability of citric acid to form stable complexes with metal ions [5].

It has been found that in some catalytic methods for determination of heavy metals, this

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acid acting both as buffer and as complexing agent, suppresses interference from the catalytic action of a large number of metal and non-metal ions and at the same time enhances the catalytic action of the metal being determined [4].

However, it is frequently necessary to use, in such analytical methods, non-aqueous or mixed organic-water solvent systems because of the insolubility of one or more of the reactants in water. The stability constants of the various chelate compounds of citric acid in these media provide a measure of the masking effect of the acid, but in the determination of these constants it is necessary to know the dissociation constants of citric acid in the medium concerned and these are not frequently available in literature. Therefore it was aimed to study the dissociation constants of citric acid in mixed solvent systems (dioxane-water, methanol-water, ethanol-water, acetonitrile-water). The effect of temperature on dissociation constants of citric acid was also studied.

The dissociation constants ( $pK_a$ ) of weak acids and bases are widely used in pharmaceutical industries, in spectroscopy, in biological sciences, in preparative chemistry and in structure elucidation of newly isolated species [6,7].

There are different methods [8-12] which are being used for the determination of dissociation constants of weak acids and bases. These methods have certain limitations. Such as solubility, range of  $pK_a$ , time requirements etc. [10-13]. The quick method for this purpose is potentiometry [8,14] while spectrophotometry is very accurate but it is time consuming [12,15].

There is still possibility to work on determination of dissociation constants of biologically important substances where data on various temperatures and in different solvents is not available [6,7,14, 16-19].

### Theory

The  $pK_a$  values were calculated by means of a generalized form of Speakman's method [20] derived for the case of polyprotic acids with overlapping ionization steps [20]. For triprotic acids this leads to the equation:

$$\frac{h (a^*_{H})^3 y_3}{(3-h) y_0} = K_1 K_2 K_3 + K_1 K_2 \frac{(2-h) y_3 a^*_{H}}{(3-h) y_2} + K_1 \frac{(1-h) y_3 (a^*_{H})^2}{(3-h) y_1} \dots\dots\dots(1)$$

where

$$h = \frac{[Na^+] + [H^+] - [OH^-]}{C} \dots\dots\dots(2)$$

$Y_0$ ,  $Y_1$ ,  $Y_2$  and  $Y_3$  being the activity coefficient of the species  $H_3C_i$ ,  $H_2C_i^-$ ,  $HC_i^{2-}$  and  $C_i^{3-}$  respectively,  $C$  the analytical concentration of  $H_3C_i$  as defined by equation (4) below, and the  $a^*_{H}$  hydrogen-ion activity referred to the standard state in the corresponding medium. For dilute acid solutions the activity coefficient  $Y_0$  is usually taken as unity and the activity coefficients of the ionic species can be estimated with Debye-Huckel equations:

$$\log y_i = \frac{A Z_i^2 I^{1/2}}{1 + B a_i I^{1/2}} \dots\dots\dots(3)$$

Where  $A$  and  $B$  are the Debye-Huckel constants, the values of which depend on the physical properties of the medium [14],  $I$  is the ionic strength of the solution, and  $a$  the distance of closest approach of the ion. It should also be noted that the concentration of hydroxide ions is usually negligible in comparison with  $[Na^+]$  or  $C$  except at very high values [21]. When this is the case (acidic solutions), the average number of protons removed from the citric acid molecules, denoted by  $h$  is, equal to:

$$h = \frac{[Na^+] + [H^+]}{C}$$

This quantity can be calculated by assuming  $[H^+] \cong a^*_{H}$ . At any point of the titration curve, material balance for citric acid and the requirement of electroneutrality are expressed by the equation:

$$C = [H_3Ci] + [H_2Ci^-] + [HCi^{2-}] + [Ci^{3-}] \dots\dots\dots(4)$$

$$[Na^+] + [H^+] - [OH^-] = [H_2Ci^-] + 2[HCi^{2-}] + 3[Ci^{3-}] \dots\dots\dots(5)$$

Combing these equations and rearranging gives:

$$I = 3[Ci^{3-}] + [HCi^{2-}] + [Na^+] + [H^+] \dots\dots\dots(6)$$

$$[Ci^{3-}] = \frac{K'_1 K'_2 K'_3}{(a^*_H)^3} [H_3Ci] \dots\dots\dots(7)$$

$$[HCi^{2-}] = \frac{K'_1 K'_2}{(a^*_H)^2} [H_3Ci] \dots\dots\dots(8)$$

$$[H_2Ci^-] = \frac{K'_1}{(a^*_H)} [H_3Ci] \dots\dots\dots(9)$$

$$[H_3Ci] = \frac{C}{D} \dots\dots\dots(10)$$

where

$$D = 1 + \frac{K'_1}{a^*_H} + \frac{K'_1 K'_2}{(a^*_H)^2} + \frac{K'_1 K'_2 K'_3}{(a^*_H)^3} \dots\dots\dots(11)$$

$K'_1$ ,  $K'_2$  and  $K'_3$  being the apparent dissociation constants. The thermodynamic constants  $K_1$ ,  $K_2$  and  $K_3$  can be obtained, by a multiple linear regression method, from the coefficients of equation (1), which is rewritten as:

$$Y = K_1 K_2 K_3 + K_1 K_2 X_1 + K_1 X_2 \dots\dots\dots(12)$$

In this treatment calculations of  $Y$ ,  $X_1$  and  $X_2$  require for knowing the value of  $K'_1$ ,  $K'_2$  and  $K'_3$ . These apparent constants can be derived from equation (12) as described before, by putting  $Y_1$ ,  $Y_2$  and  $Y_3$  equal to 1. We can mark here that  $Y = (X_1, X_2)$  was always found to be linear ( $R^2 > 0.999$ ) in the neutralization range between 20 and 80%.

In an attempt to test the accuracy of the present method, the thermodynamic  $pK_n$  values of

citric and in aqueous solutions obtained,  $pK_1 = 3.112$ ,  $pK_2 = 4.442$  and  $pK_3 = 5.836$  are very close to the reported  $pK_n$  values at 25°C [8].

**Results and Discussion**

The protonation constants of citric acid were determined in water at 25, 30, 35, 40, 45 and 50°C and in 10, 20, 30 and 40 percent organic-water solvent mixture at 25°C. The protonation constant of citric acid were obtained by refining the experimental data with the aid of Computer Program PKAS [22].

The  $pK_n$  values calculated are presented in Table-1 together with the reported value at 25°C which agree reasonably with the reported values.

Table-1:  $pK_n$  values and thermodynamic constants of citric acid at different temperature

Temp °C	$pK_n$ Evaluated	$pK_n$ Reported	$\Delta G$ kcal/mol	$\Delta H$ kcal/mol	$\Delta S$ cal/mol/K
25	3.112	3.08	4.245	16.427	40.860
	4.442	4.39	6.060	7.531	4.938
	5.836	5.89	7.961	5.923	6.835
30	2.948		4.089	16.475	
	4.324		5.998	7.494	
	5.696		7.901	5.828	
35	2.781		3.921	16.512	
	4.247		5.988	7.509	
	5.637		7.948	5.841	
40	2.598		3.722	16.517	
	4.163		5.965	7.511	
	5.582		7.998	5.857	
45	2.394		3.485	16.845	
	4.084		5.945	7.515	
	5.523		8.040	5.864	
50	2.171		3.210	16.414	
	4.007		5.924	7.520	
	5.487		8.113	5.903	

Increase in temperature causes decrease in  $pK_n$  values but this decrease is not same for all the three ( $pK_1$ ,  $pK_2$ ,  $pK_3$ ) values. As temperature increases from 25 to 50°C,  $pK_1$  value drops from 3.112 to 2.171,  $pK_2$  values from 4.442 to 4.002 and  $pK_3$  values from 5.836 to 5.487 and total decrease are 0.941, 0.435 and 0.349 units for  $pK_1$ ,  $pK_2$  and  $pK_3$  respectively. Fig. 1 further clarify the effect. Fig. 2 shows the effect of temperature on Gibb's free energy changes in thermodynamic functions

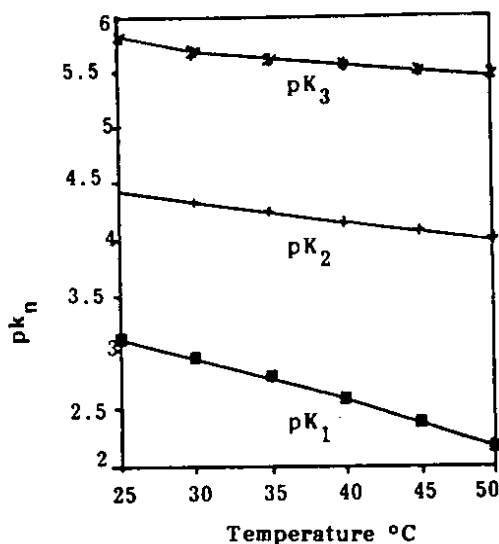


Fig. 1: Effect of temperature on pK<sub>n</sub> values of citric acid.

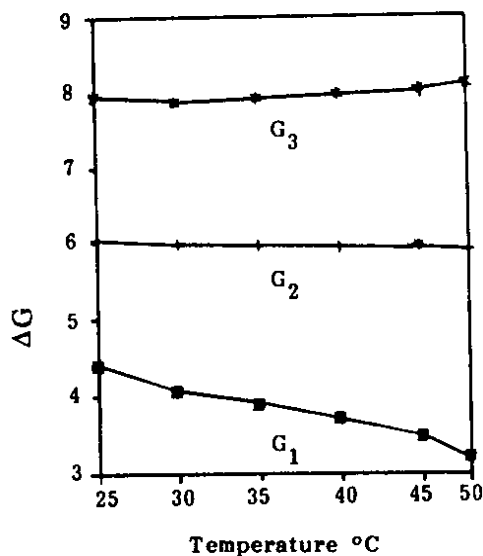


Fig. 2: Effect of temperature on ΔG<sub>n</sub> values of citric acid.

ΔG, ΔH and ΔS at 25°C have been calculated by using eq (13) [23].

$$pK = \frac{\Delta H}{RT} - \frac{\Delta C_p}{R} \cdot \ln T - \frac{\Delta S}{R} + \frac{\Delta C_p}{R} \quad \dots (13)$$

If C<sub>p</sub> is zero over the temperature range investigated the above equation reduces as

$$pK = \frac{\Delta H}{RT} - \frac{\Delta S}{R}$$

where

$$\Delta G = \Delta H - T \Delta S$$

Many chemist require to know the dissociation constants of organic acids and bases in non-aqueous media. Therefore in recent years much attention has been paid to a quantitative explanation of the medium on pK<sub>n</sub> values [24-30].

In recent years many non-aqueous solvents have been increasingly used in analytical chemistry. They are generally organic solvents and may be used as mixture, with each other or with water. For this reason it is interesting to compare their behaviour with that of water. One of the most important property of a solvent is its dielectric constant, which defines to a considerable degree of the solvating ability of the medium [9].

Solvents may be distinguished according to their dielectric constant value and also their tendency to form hydrogen bonds. Both these properties were taken into consideration and we selected four solvent (dioxane, methanol ethanol and acetonitrile). Selection of these solvents based on the fact that water, ethanol and methanol are the solvents having dielectric constant values 78.5, 32.6 and 24.3 respectively and also having ability to form hydrogen bond while acetonitrile and dioxane having dielectric constant values 36.0 and 2.21 respectively but have no ability to form hydrogen bonds.

There is considerable difference in the solvating ability of the two groups. In order to measure the effect of these two groups on pK<sub>n</sub> values of citric acid we extended our investigation. The influence of the nature of the solvent and composition of the medium on dissociation equilibria was studied.

Fig. 3. shows the effect of percent composition of dioxane-water, ethanol-water, methanol-water and acetonitrile-water solvent system on pK<sub>1</sub> values. As percent composition of organic-water mixture increases from 0 to 40 than pK<sub>1</sub> values also increase but increase in value is not

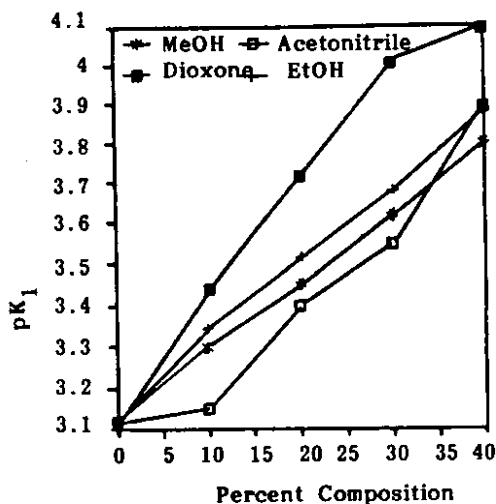


Fig. 3: Effect of organic-water solvent mixture on pK<sub>1</sub> values of citric acid.

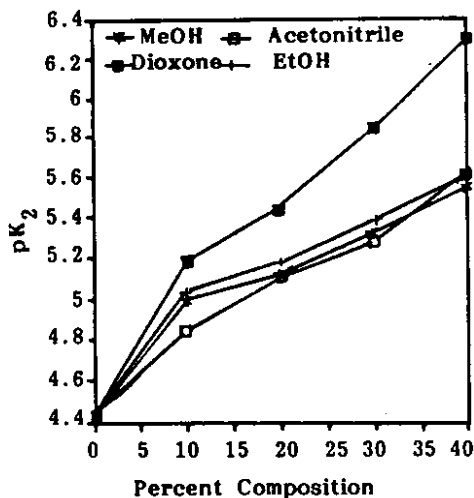
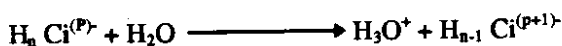


Fig. 4: Effect of organic-water solvent mixture of pK<sub>2</sub> values of citric acid.

same. In dioxane-water and acetonitrile-water solvent system total increase in pK<sub>1</sub> value is 0.94 and 0.72 unit respectively while in methanol-water and ethanol-water solvent system increase is 0.50 and 0.53 unit respectively. This shows that in solvents (methanol and ethanol) forming hydrogen bonding, increase in pK value is much higher. Nearly same effect is observed for pK<sub>2</sub> and pK<sub>3</sub> values in mixed solvent system (Fig. 4 and 5).

It was measured that these effect could be described by simple equations for the dependence of pK<sub>n</sub> on a particular variable related to the solvent composition. The bulk dielectric constant D of the solvents is usually used for this purpose so pK<sub>n</sub> = f (1/D) or pK<sub>n</sub> vs % composition can be plotted. It was also assumed from the literature [21] that in water rich mixtures the proton probably occurs as a hydronium ion, regardless of the nature of organic solvents. Consequently, the ionization reactions are



Where p+n = 3. The acidity constants of these reactions explicitly include the activity of water

$$K_n^{\circ} = \frac{K_n}{a_{H_2O}}$$

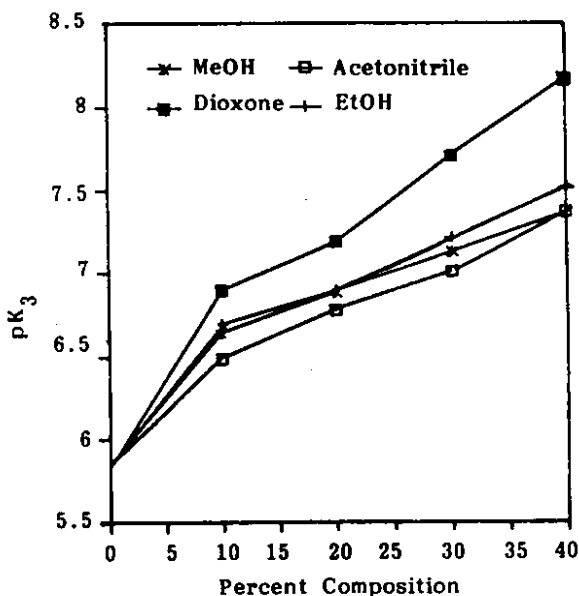


Fig. 5: Effect of organic-water solvent mixture on pK<sub>3</sub> values of citric acid.

where a<sub>H<sub>2</sub>O</sub> can be approximated by its concentration.

The graph pK<sub>n</sub><sup>∘</sup> = f (1/D) or pK<sub>n</sub> vs % composition of solvent are theoretically justified in terms of following equation, based on Born's electrostatic model [21].

$$\frac{dpK_n^{\circ}}{d(1/D)} = \frac{e^2}{2k \Gamma(\ln 10)} \phi_n \quad (14)$$

Where  $\phi_n$  is expressed in terms of the reciprocal of the radii of the ions taking part on the equilibrium,  $k$  is the Boltzman constant and  $T$  is the absolute temperature. For  $n$  equal to 1 or 2 we have

$$\phi_1 = \frac{1}{r_H} + \frac{1}{r_1} \text{ and } \phi_2 = \frac{1}{r_H} + \frac{4}{r_2} - \frac{1}{r_1}$$

Where  $r_H$ ,  $r_1$  and  $r_2$  being the radii of  $H^+$ ,  $H_2Cl^+$  and  $HCl_2^+$  respectively.

Eq (14) predicts a linear relationship between  $pK$  (1/D) in all cases for which changes in  $pK_n$  after change of medium can be attributed to electrostatic phenomena.

In each mixture, it was observed that the graph  $pK$  vs % composition of solvent-water for  $pK_1$ ,  $pK_2$ ,  $pK_3$  are markedly different. These finding leads to the conclusion that the non-electrostatic solute-solvent interactions for citric acid depend markedly on the nature of the organic component of solvent mixtures.

### Experimental

Reagent grade citric acid (Merck GR) which was dried in vacuum for overnight was used. The purity of acid was checked by potentiometric titration. The acid solution of initial concentration 0.01 M were prepared by direct weighing and dissolution in 50 ml  $H_2O$ , just before use. The titrant 0.1 M sodium hydroxide solution (Carbonate free standardized with potassium hydrogen phthalate) was prepared in water and also in mixed solvents.

Double distilled deionized water ( $1.0 \times 10^{-6} \Omega^{-1} \text{ cm}^{-1}$  conductivity) was used throughout the experiment. Ethanol, methanol, dioxane and acetonitrile used were also purified [31].

Prior to experiment, pH-meter was calibrated with known buffer of potassium hydrogen tartrate (pH at 25°C is 3.557) potassium hydrogen phthalate (pH at 25°C is 4.005) and dihydrogen phosphate (pH at 25°C is 6.865) [32] in respective solvents.

The Philips PW 9420 digital pH-meter coupled with ingold combined glass and Ag/AgCl reference in double walled glass cell was kept constant by circulating water from JULABO HC. Thermostat bath accurate to  $\pm 0.01^\circ\text{C}$ . Mettler DV 210 micro burette readable to  $\pm 0.01$  ml was used as dispenser of titrant. Before and during measurement sample solution was kept at inert atmosphere by bubbling purified nitrogen gas.

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