# Determination of Ionization Constants of Substituted Phenols by Potentiometry and Liquid Chromatography

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Summary: Ionization constants of phenol, p-cresol and orthochlorophenol have been determined at varying temperature from 25 to 50°C and in 10, 20, 30 and 40 percent methanol-water solvent system at 25°C by potentiometry. $pK_a$ values of all these compounds also been determined in varying percentage of methanol-water solvent system by liquid chromatography on a reversed phase column at 25°C. The purpose of this investigation was to obtain the data for the dissociation of phenol derivative using diverse methods with particular emphasis on the effect of chloro (-Cl) and methyl (-CH₃) group on phenyl ring which in turn effect on $pK_a$ values. Results obtained by both methods were compared and effect of substituents on phenyl ring is being discussed in light of Hammets equations. Potentiometric data was analysed by computer program written in GW-BASIC for calculation of pK values.

## Introduction

The present study is a continuation of our previous work which describes the method for the determination of ionization constants of acids and bases [1-3].

The value of the ionization constant of chlorinated phenolic compounds is an important property to note when considering the potential transfer of these compounds to sediments and biological tissues. The determination of ionization constant of phenol and its derivative has been the subjected of many investigations [4-6].

There are different methods [7-13] which were being used for the determination of dissociation constants of weak acids and bases.

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These methods have certain limitations such as solubility, range of pK$_a$, time requirement etc. The quick method for this purpose is potentiometry while spectrophotometric method is very accurate but it is time consuming. Liquid chromatographic method has definite advantage over other methods that 1 mg or less of the substance is needed for determination of acidity constant and that the purity of substance is not critical as the impurity can be separated from the substance on the reversed phase column [14].

The survey of literature shows that the ionization constant of chlorinated phenolic compounds have been studied by William C. Purdy and co-workers [14] but effect of temperature and solvent on pK$_a$ values and effect of substitution of chloro and methyl group on phenyl ring is not studied.

It has been the aim of the present investigation to obtain the data on effect of temperature and solvent composition (methanol-water) on pK$_a$ values of phenol, orthochlorophenol and p-cresol using potentiometric data. pK$_a$ values of these compounds have also been determined in 40, 50, 60, 70 and 80 percent methanol-water solvent system using high performance liquid chromatography. Results obtained by both methods are compared and agreed reasonably with the few reported results [10,14]. An attempt has been made to view the effect of substitution on phenyl ring when electron with-drawing group (-Cl) and electron donating group (-CH$_3$) is substituted on phenol, how does it effect on pK$_a$ values.

Potentiometric data was analysed by computer program written in GW-BASIC for calculation of pK$_a$ values of monobasic acids.

*Theory*

Any monobasic acid HA dissociates as follows:-

$$HA \rightleftharpoons H^+ + A^-  \qquad (1)$$

$$K^C_a = \frac{[H^+] + [A^-]}{[HA]} \qquad (2)$$
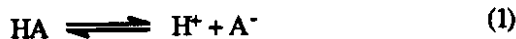
$$pK^C_a = pH + Log \frac{[HA]}{[A^-]} \qquad (3)$$

Where the term in square bracket represent [ ] molar concentration. K$_a$ is the concentration ionization constant. When titrating an acid with base, electric neutrality gives

$$[A^-] + [OH^-] = [Na^+] + [H^+] \qquad (4)$$

Or     $$[A^-] = [Na^+] - [OH^-] + [H^+] \qquad (5)$$

If Co is the total ion concentration of acid taken, then

$$Co = [A^-] + [HA] \qquad (6)$$

$$[HA] = Co - [A^-] \qquad (7)$$

Substituting the values of [A$^-$] from Eq (5) in Eq(7), we get

$$[HA] = CO - [Na^+] + [OH^-] - [H^+] \qquad (8)$$

Eq (3), Eq (5) and Eq (8) have been used to calculate pK$_a$ values using no approximation.

The general formulation of the relationship between the concentration of an ion C$_i$ and its activity Coefficient Y$_i$ is based on the work of Debye-Hückel [9]. An important term in the formulation is the ionic strength, written as I and is defined as

$$I = 0.5 \, \Sigma \, C_i Z^2$$

Where C$_i$ is the molecular concentration of an ion and Z is its valency and $\Sigma$ denotes summation. According to Debye-Hückel, the activity coefficient Y$_i$ of an ion of valency Z is related to the ionic strength.

$$-Log \, Yi = \frac{A \, Z_i^2 \, I^{0.5}}{I + Ba_i \, I^{0.5}} \qquad (9)$$

The term A and B are Debye-Hückel constants which vary with the dielectric constant and temperature of the solvent [9]. The term a$_i$ is the ionic size parameter, that is the mean distance

of approach of the ions, for which $4.5 \times 10^{-8}$ cm may be taken as an average value. The thermodynamic ionization or dissociation constants can be written as [10].

$$K_a^T = \frac{\{H^+\}[A^-]}{\{HA\}} \ Y_{A^-} \qquad \text{For acid} \quad (10)$$

and

$$K_a^T = \frac{\{H^+\}\{B\}}{[BH^+]} \ \frac{1}{Y_{BH^+}} \qquad \text{For bases ...}(11)$$

In which the term $Y_{A^-}$ and $Y_{BH^+}$ are the respective activity coefficients calculated by means of Eq(9) and term in { } are activities of respective ions. Hence at temperature 20°C concentration ionization constant ($pK_a^c$) can be converted to thermodynamic ionization constant ($pK_a^T$) by using Eq (3) [3].

$$pK_a^T = pK_a^c + \frac{0.507 \ I^{0.5}}{1 + 1.5 \ I^{0.5}} \qquad \text{For acids} \quad (12)$$

$$pK_a^T = pK_a^c - \frac{0.507 \ I^{0.5}}{1 + 1.5 I^{0.5}} \qquad \text{For bases} \quad (13)$$

*Theory of liquid chromatography*

The dissociation of a monoprotic acid, HA in the mobile phase is governed by the following equilibrium [14]

$$HA \longrightarrow A^- + H^+ \quad \cdots\cdots\cdots\cdots \quad (1)$$
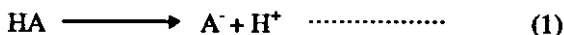
Where $A^-$ is the dissociation acid and $H^+$ is the solvated proton. The equilibrium constant is the acid dissociation constant in the eluent proper, $K_{am}$, and is given by

$$K_{am} = \frac{[H^+]_m [A^-]_m}{[HA]_m} \qquad (2)$$

where $[H^+]_m$, $[A^-]_m$, and $[HA]_m$ are the concentrations of the solvated proton, the dissociated, and undissociated acid in the mobile phase, respectively.

In the chromatographic process under consideration, solute retention is assumed to occur because of a reversible association between the dissociated and/or undissociated acid and the hydrocarbonaceous ligand. L, of the stationary phase. The binding of the acid is determined by the equilibrium

$$HA + L \longrightarrow LHA \qquad (3)$$

With the equilibrium constant $K_{LHA}$ which is given by

$$K_{LHA} = \frac{[LHA]_s}{[HA]_m [L]_s} \qquad (4)$$

Where $[LHA]s$ and $[L]s$ are the concentrations of the complex LHA and the ligand of the stationary phase $[L]_s$ respectively.

The interaction between the anion and the ligand results in the formation of the complex $LA^-$ according to the following equilibrium

$$A^- + L \longrightarrow LA^- \qquad (5)$$

and the corresponding equilibrium constant $K_{LA^-}$ is given by

$$K_{LA^-} = \frac{[LA^-]_s}{[A^-]_m [L]_s} \qquad (6)$$

where $[LA^-]_s$ is the concentration of the complex in the stationary phase.

The magnitude of solute retention is expressed by the capacity factor k, which is measured of the stoichiometric mass distribution of HA between the stationary and mobile phases. In a given column the volume ratio of the stationary and mobile phases, $\phi$ is fixed so that the mass distribution ratio is simply given by

$$k = \phi \ \frac{[LHA]_s + [LA^-]_s}{[HA]_m + [A^-]_m} \qquad (7)$$

Expressing the species concentration from Eq. (2), (4) and (5) and substituting into Eq. (7), was obtain the capacity factor as

$$k = \phi \cfrac{K_{LHA}[L]_s + K_{LA^-}[L]_s \cfrac{K_{am}}{[H^+]_m}}{1 + \cfrac{K_{am}}{[H^+]_m}} \qquad (8)$$

It is convenient to define the capacity factor of the undissociated acid, $k_0$ as

$$k_0 = \phi [L]_s K_{LHA} \qquad (9)$$

and the capacity factor of the conjugate base $k_{-1}$, as

$$k_{-1} = \phi [L]_s K_{LA^-} \qquad (10)$$

Substituting $k_0$ and $k_{-1}$, from Eq. (9) and Eq. (10) into Eq. (8), we obtain for the capacity factor of a monoprotic acid the following expression

$$k = \cfrac{k_0 + k_{-1} \cfrac{K_{am}}{[H^+]_m}}{1 + \cfrac{K_{am}}{[H^+]_m}} \qquad (11)$$

## Results and Discussion

Dissociation constants for phenol, p-cresol and orthochlorophenol were determined by potentiometry and liquid chromatography. The $pK_a$ values of these compounds were determined from the corresponding titration of 50 ml of solution of each compound with 0.1 M sodium hydroxide using potentiometric data.

Results summarized in Table-1 using potentiometric data show that as temperature increases from 25 to 50°C, $pK_a$ values of phenol, p-cresol and orthochlorophenol decrease from 9.92 to 9.58, 10.10 to 9.69 and 9.07 to 8.65 and total decrease in values are 0.34, 0.41 and 0.42 for phenol, p-cresol and orthochlorophenol respectively. It is clear that effect of temperature on $pK_a$ value is nearly the same for substituted and unsubstituted phenol, $pK_a$ values measured at 25°C is close to the reported $pK_a$ values at this temperature.

Table-1: Effect of temperature on $pK_a$ values in aqueous media using potentiometric data.

| Temp. °C | Phenol $pK_a$ | | p-Cresol $pK_a$ | | Monochlorophenol $pK_a$ | |
|---|---|---|---|---|---|---|
| | * | ** | * | ** | * | ** |
| 25 | 9.92 | 10.0 | 10:10 | 10.15 | 9.07 | 9.13 |
| 30 | 9.81 | | 10.05 | | 9.03 | |
| 35 | 9.76 | | 9.97 | | 8.94 | |
| 40 | 9.70 | | 9.87 | | 8.83 | |
| 45 | 9.62 | | 9.76 | | 8.76 | |
| 50 | 9.58 | | 9.69 | | 8.65 | |

* = $pK_a$ Evaluated, ** = $pK_a$ Reported

Effect of solvent on $pK_a$ values has also been studied in varying percentage of methanol-water solvent system and results are shown in Table 2a. This table makes it clear that as composition of solvent increases from 10 to 40 percent, $pK_a$ values for all investigated compounds increase linearly and total increase in $pK_a$ values are 0.09, 0.1 and 0.12 for phenol, p-cresol and orthochlorophenol respectively. Again this help to view that the effect of solvent on $pK_a$ values is same for substituted and unsubstiuted phenols.

Table-2a: Effect of solvent on $pK_a$ values using potentiometric data

| Compound | Percent Composition of Methanol-water | | | |
|---|---|---|---|---|
| | 10 | 20 | 30 | 40 |
| Phenol | 9.94 | 9.97 | 9.99 | 10.03 |
| p-Cresol | 10.14 | 10.16 | 10.19 | 10.23 |
| Monochlorophenol | 9.09 | 9.12 | 9.16 | 9.21 |

Liquid chloromatographic investigation summarized in Table 2b shows that as composition of mobile phase (methanol) increases from 40 to 80 percent then again $pK_a$ values increase linearly. Increase in $pK_a$ values with increasing methanol concentration is a result of change in dielectric constant of solvent which is in accordance with the theory. The dielectric constant of solvent is measure of how well that solvent can separate oppositly charged ions. According to Coulomb's

Table-2b: Effect of solvent on $pK_a$ values using liquid chromatographic data.

| Compound | Percent Composition of Methanol-water | | | | |
|---|---|---|---|---|---|
| | 40 | 50 | 60 | 70 | 80 |
| Phenol | 10.00 | 10.03 | 10.12 | 10.19 | 10.30 |
| p-Cresol | 10.18 | 10.22 | 10.28 | 10.37 | 10.50 |
| Monochlorophenol | 19.17 | 9.22 | 9.29 | 9.38 | 9.52 |

law [15] the attraction force between two ions of charge q⁻ and q⁺ separated by a distance 'r' is

$$F = 8.988 \times 10^9 \ \frac{q^- \cdot q^+}{\varepsilon \, r^2}$$

Where $\varepsilon$ is the dielectric constant of the solvent. The attraction forces is inversely proportional to the dielectric constant. The larger the value of the dielectric constant, the smaller the attraction between two ions ($H^+$ and $A^-$ for dissociation reaction $HA \rightarrow H^+ + A^-$) and thus the larger the acidity constant [13].

In this case, the dielectric constants of water and methanol are 78.5 and 31.5 respectively [16]. With an increase in methanol concentration the dielectric constant of the solvent will decrease resulting in a decrease of acidity constant or an increase in $pK_a$ values.

Table-2b shows that as percent composition of methanol-water increases from 40 to 50 then there is minimum increase in $pK_a$ value but when methanol concentration increases from 70 to 80 percent then sizable increase in $pK_a$ values has been marked.

A closer inspection of Tables 2a and 2b shows that, $pK_a$ values of phenol, p-cresol and orthochorophenol measure in 40 percent methanol using potentiometric and liquid chromatographic method, are very close to each other. $pK_a$ value of phenol determined by potentiometry in 40 percent methanol is 10.03 while it is 10.0 in same percentage of methanol by liquid chromatography, for p-cresol $pK_a$ value measured by potentiometry is 10.23 while 10.18 by liquid chromatography. likewise $pK_a$ values of orthochorophenol are 9.21 and 9.17 by potentiometry and liquid chromatography respectively.



Phenol          p-Cresol          o-Chlorophenol
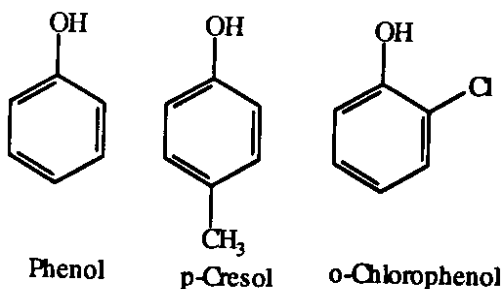
Data listed in Table-1 cleary indicate that $pK_a$ value of unsubstituted phenol is 9.92 but for p-cresol when methyl group is substituted at para position then $pK_a$ value increase upto 10.10, when chloro group is substituted in phenyl ring at ortho position then $pK_a$ values drop to 9.07. These finding are in accordance with the Hammett equation [17].

$$\text{Log } K_i - \text{Log } K_o = \rho \delta$$

Where $K_o$ is the acidity constant of unsubstituted acid and $K_i$ is the acidity constant of substituted acid. The parameter $\rho$ is called the reaction constant, which is different for each substrate. According to Hammette's equation, electron-withdrawing substituents (-Cl group) increase the ionization constant or decrease the $pK_a$ values and thus have positive $\delta$ value, while electron-donating group (-CH₃) decrease the ionization constant or increase the $pK_a$ values and have negative $\delta$ value.

Keeping in view the Hammett's equation we can say that results presented in Tables-1 and 2 clearly shows that the $pK_a$ values of p-cresol is higher than phenol because of the effect of electron-donating group and $pK_a$ value of orthochlorophenol is lower than the phenol because of electron-withdrawing group, so we can say that nature of substituents has notable effect on $pK_a$ values.

**Experimental**

All chemicals were of analytical grade and used without further purification. Double distilled carbon dioxide free water was used throughout the study. Fresh distilled methanol was used. Stock solution of 0.1 M sodium hydroxide and 0.2 M phenol, 0.01 M p-cresol and 0.1 M orthochloro-phenol were prepared in $CO_2$ free distilled water. Phenol, p-cresol and orthochlorophenol were first dissolved in 1% alcohol and then the concentration was maintained upto mark with water. The solution of compounds was kept in a cell coupled with Ingold combined glass and Ag/Agcl reference electrode. The glass electrode was calibrated with borax buffer (pH = 9.180 at 25°C) and sodium hydrogen carbonated (pH = 10.012 at 25°C [18]. The temperature of the solution was maintained

constant by circulating water from JULABO HC theromostate bath accurate to 0.01°C through double jacket cell. The pH of solution was measured with PHILIPS PW 9420 digital pH meter. Mettler DV 210 micro burette readable to $\pm$ 0.01 ml was use as dispenser of titrant. Effecient mixing of sample was obtained by magnetic stirrer. Before and during measurement sample was kept at inert by bubbling purified nitrogen gas. The experimental data obtained was analysed by computer program in GW-BASIC. Hitachi model liquid chromatograph comprises a L-6200 intelligent pump, UV-VIS L-4200 detector analytical column liqrosorb $RPC_{18}$ was used for chromatographic data. HPLC grade methanol used was obtained from Fluka.

Phenol p-cresol and orthochlorophenol were dissolved in 1% alcohol and solution of compounds were prepared to give final concentration 1 $\mu g/\mu l$ 1$\mu l$ of all solutions were injected. Phosphoric acid and sodium phosphate buffers of 0.02 M ionic strength were used. Composition of mobile phase (methanol) was increased from 40 to 80% with flow rate of 1 ml/min at column temperature 25°C.

pK$_a$ values were obtained by plotting pH vs capacity factor (k). The mid point of the sigmoidal curve is the pK$_a$ value of the compound. Capacity factor was determined by equation which was derived by Horvath *et al.* [19].

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