

A Computational Method for Calculation of Dissociation Constants of Benzoic Acid and Sodium Benzoate

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Summary: The experimental potentiometric data have been used for the determination of thermodynamic dissociation constants of benzoic acid and sodium benzoate. A computer program in GW-BASIC has been used to calculate the dissociation constants pK_a values of these substances from experimental data. The effect of temperature, solvents and solvent composition on dissociation constant pK_a values has also been carried out. The pK_a values are as follows:

Temperature °C	Composition %	Benzoic acid	Sodium Benzoate
25	aqueous	4.184 ± 0.010	4.065 ± 0.008
50	aqueous	4.293 ± 0.009	3.506 ± 0.005
25	10% dioxane-water	4.600 ± 0.004	4.352 ± 0.009
25	40% dioxane-water	5.190 ± 0.010	5.041 ± 0.009
25	10% methanol-water	4.651 ± 0.003	4.404 ± 0.007
25	40% methanol-water	4.882 ± 0.005	4.541 ± 0.010
25	10% ethanol-water	4.681 ± 0.005	4.510 ± 0.007
25	40% ethanol-water	4.864 ± 0.006	4.643 ± 0.010

Introduction

The dissociation constant (pK_a) of weak acids and bases is widely used in pharmaceutical industries, in spectroscopy, in biological sciences, in preparative chemistry and in structure elucidation of newly isolated species [1,2].

There are different methods [3-6] 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. [4,7]. The quick method for this purpose is potentiometry [3-8] while spectrophotometric method is very accurate but it is time consuming [4-7].

There is still possibility to work on determination of dissociation constants of biologically important substances where data on various temperatures and in different solvent is not available [2,3,9-12].

The potentiometric titration has been improved by elimination of carbon dioxide using dried and purified nitrogen gas [3], controlling temperature accuracy to ± 0.1 °C in pK_a values were obtained by analysing the experimental data with a computer program written in GW-BASIC to

work on IBM PC or compatible computers [13]. The object of this study is to determine the accurate dissociation constant (pK_a) values of pharmaceutically important substances at different temperatures and in different solvents at different solvent concentrations.

Theory

Any monobasic acid HA dissociates as follows:-



$$K_a^c = \frac{[H^+] + [A^-]}{[HA]} \quad (2)$$

$$pK_a^c = pH + \log \frac{[HA]}{[A^-]} \quad (3)$$

Where the terms in square brackets [] represent molar concentration. K_a^c is concentration ionization constant. When titrating an acid with base, electric neutrality gives

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

$$\text{or } [A^-] = [Na^+] - [OH^-] + [H^+] \quad (5)$$

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If C_0 is the total ion concentration of acid taken, then

$$C_0 = [A^-] + [HA] \quad (6)$$

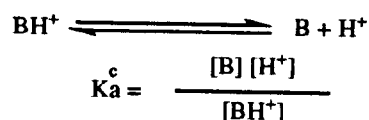
$$[HA] = C_0 - [A^-] \quad (7)$$

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

$$[HA] = C_0 - [Na^+] + [OH^-] - [H^+] \quad (8)$$

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

Any monoacidic base BH^+ dissociates as follows



Thermodynamic Constant for an acid is:

$$K_a^T = \frac{[H^+][A^-]}{[HA]}$$

and for bases this constant is:

$$K_a^T = \frac{[H^+][B]}{[BH^+]}$$

where $[A^-] = [A^-] Y_{A^-}$

$[BH^+] = [BH^+] Y_{BH^+}$

$$-\log y_i = \frac{Az^2 I^{0.5}}{1 + Ba_i I^{0.5}} \quad (9)$$

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.

A and B are constants, z is valency of ion and I is ionic strength [3].

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].

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

and

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

Results and Discussion

It has been observed that the pK_a values are temperature dependent, but there is no rule whether the pK_a values will increase or decrease with the increase in temperature. In case of benzoic acid when temperature increases from 20°C to 30°C, pK_a values decrease but when the temperature further increases upto 50°C, the pK_a values also increases (Table 1 and Fig. 1) but in case of sodium benzoate as the temperature increases, pK_a values continuously decrease (Table 2 and Fig. 2).

Table-1: Effect of temperature on pK_a values and thermodynamic constants of benzoic acid

Temp. °C	pK_a^c	pK_a^T	ΔG kcal/mol	ΔH kcal/mol	ΔS cal/mol/K
20	4.17 ± 0.004	4.202 ± 0.007	5.636	-1.496	-24.32
25	4.153 ± 0.006	4.184 ± 0.009	5.708	-1.546	
30	4.111 ± 0.004	4.143 ± 0.006	5.746	-1.629	
35	4.167 ± 0.004	4.199 ± 0.009	5.920	-1.547	
40	4.210 ± 0.007	4.242 ± 0.005	6.077	-1.541	
45	4.221 ± 0.005	4.253 ± 0.008	6.191	-1.549	
50	4.260 ± 0.005	4.293 ± 0.009	6.347	-1.514	

Table-2: Effect of temperature pK_a values and thermodynamic constants of sodium benzoate

Temp. °C	pK_a^c	pK_a^T	ΔG kcal/mol	ΔH kcal/mol	ΔS cal/mol/K
20	4.138 ± 0.005	4.106 ± 0.009	5.508	9.334	13.053
25	4.096 ± 0.007	4.065 ± 0.00	5.545	9.437	
30	3.992 ± 0.006	3.959 ± 0.010	5.491	9.448	
35	3.902 ± 0.009	3.869 ± 0.010	5.455	9.477	
40	3.754 ± 0.005	3.720 ± 0.008	5.330	9.417	
45	3.959 ± 0.008	3.561 ± 0.005	5.185	9.336	
50	3.541 ± 0.007	3.506 ± 0.005	5.185	9.402	

The effect of different solvents and solvent concentration on pK_a values is significant. Generally the pK_a values increase as the concentration of solvent increases from 10% to 40% (Fig. 3 and 4). Dielectric constant also has an

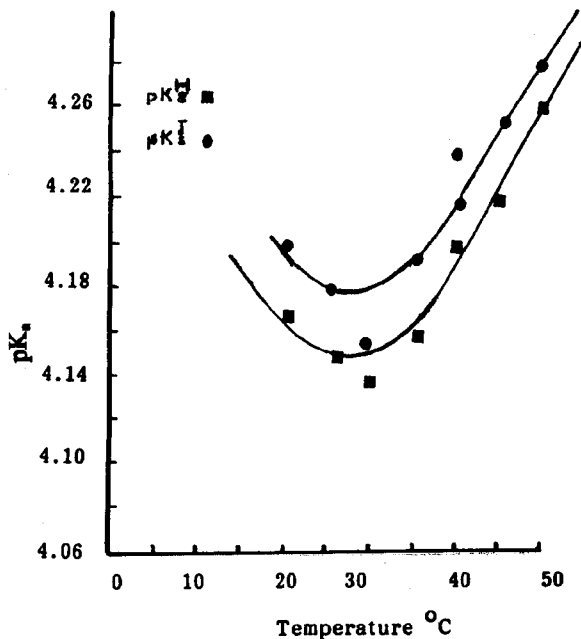


Fig. 1: Graph showing the variation in concentration ionization constant pK_a^c and thermodynamic ionization constant pK_a^T of benzoic acid with temperature.

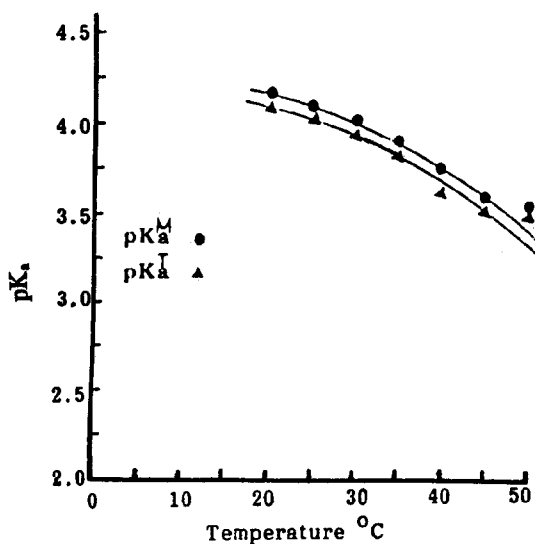


Fig. 2: Effect of temperature variation on pK_a^T values of benzoic acid in 10 to 40% concentration of dioxane, ethanol and methanol.

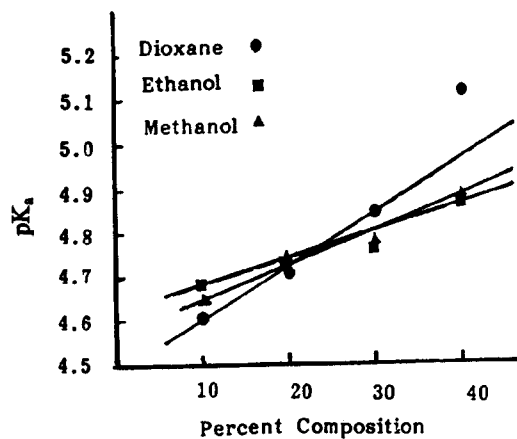


Fig.3: Graph showing the variation in pK_a^T values of benzoic acid in 10 to 40% concentration of dioxane, ethanol and methanol.

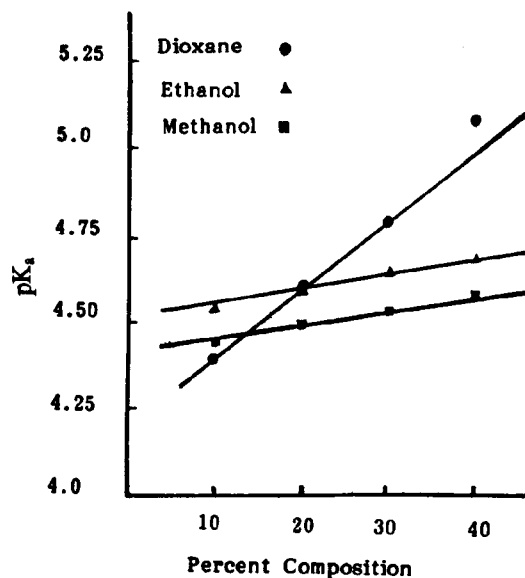


Fig.4: Graph showing the variation in pK_a values of sodium benzoate in different concentration of dioxane, ethanol and methanol.

effect on pK_a values, because in case of benzoic acid and sodium benzoate it is observed that pK_a values increase when solvent having low dielectric constant value is used.

The results obtained after some improvement in measuring technique are accurate, reproducible and comparable to some of reported pK_a values [14]. All the results were obtained by analysing the experimental data on computer program written in GW-BASIC language [15]. The values obtained for thermodynamic functions are in good argument with the few values reported in the literature. Moreover the changes in thermodynamic function ΔG , ΔH and ΔS at 25°C have been calculated by using Eq (14) [16].

$$pK_a^T = \frac{\Delta H}{RT} - \frac{\Delta C_p}{R} \log_e T - \frac{\Delta S}{R} + \frac{\Delta C_p}{R} \quad (14)$$

$$pK_a^T = \frac{\Delta H}{RT} - \frac{\Delta S}{R} \quad (15)$$

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

Percentage ionization of sample is calculated by using formula [3] given by Eq (16).

$$\% \text{ ionized} = \frac{100}{1 + 10^{(pK_a^T - pH)}} \quad \text{For acids} \quad (16)$$

$$\% \text{ ionized} = \frac{100}{1 + 10^{(pH - pK_a^T)}} \quad \text{For bases} \quad (17)$$

We can thus calculate maximum percentage ionized of a sample at particular pH.

As the temperature increases, pH changes and therefore percentage of sample ionization alters. We found that percentage of sample ionization is related with temperature which in turn is related with pH and pK_a . In case of benzoic acid there is no regular increase or decrease in pK_a^T (Table 1).

When temperature increases from 20 to 30°C then pK_a values of benzoic acid decrease and its pH also decreases but increase in temperature from 30 to 50°C shows abrupt change. pK_a^T increases and decreases pH also increases and percentage ionization of sample decreases.

In case of sodium benzoate 90.4% sample is ionized when pH is 3.12 and temperature is 20°C. When temperature increases to 50°C the percentage of sample ionization drops to only 82.6% and pH becomes 2.83 (Fig. 5).

It has also been observed that different solvents and their composition effect on percentage of sample ionization. In case of benzoic acid (monobasic acid), the percentage of sample ionization slightly decreases as composition of solvents increases from 10 to 40%, but in case of sodium benzoate (monoacidic base) percentage of sample ionization increases as the composition of solvent increases from 10 to 40%.

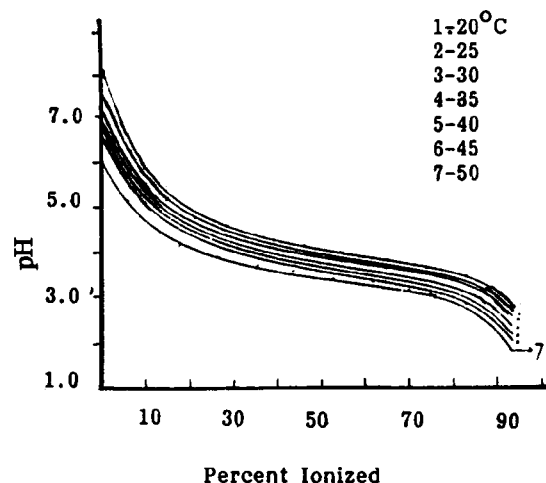


Fig.5: Graph showing the variation in percent ionization of sodium benzoate versus pH at different temperature.

Temperature also has an effect on Gibb's free energy (ΔG) Fig. 6 and 7. There is no regular increase or decrease in ΔG with the temperature. In case of benzoic acid, ΔG is 5.63 kcal/mol at 20°C but when temperature increases to 50°C, ΔG value increases linearly.

Fig. 6 shows that ΔG is minimum i.e. 5.63 kcal/mol at 20°C and becomes maximum i.e. 6.34 kcal/mol at 50°C. But in case of sodium benzoate (Fig. 7) erratic behaviour of ΔG with temperature is observed. When temperature increases from 20 to 25°C, ΔG increases from 5.50 to 5.54 kcal/mol but

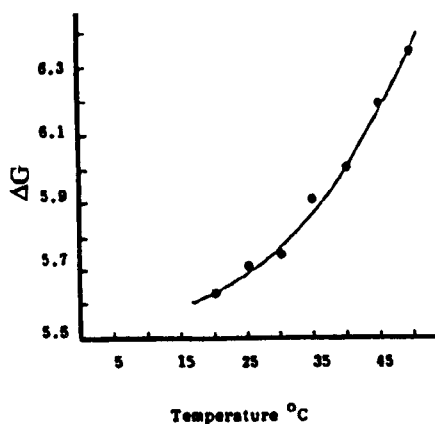


Fig.6: Graph showing the variation in ΔG of benzoic acid with temperature.

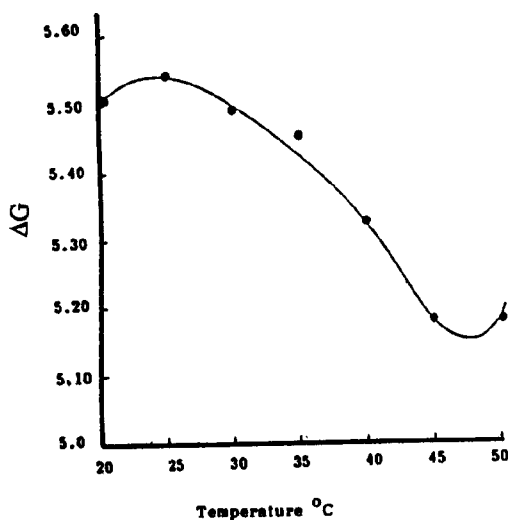


Fig.7: Graph showing the effect of temperature on ΔG of sodium benzoate.

when temperature is further increased from 25 to 45°C, ΔG is continuously decreased. When temperature is increased from 45 to 50°C, ΔG is also increased (Fig. 7 and Table 1). Fig. 8 and Fig. 9 shows the effect of solvent composition on ΔG . As the percentage composition of solvent increases from 10 to 40%, ΔG also increases linearly.

Experimental

All chemicals were of analytical grade and were used without further purification. Doubly degassed distilled water was used in preparation of all solutions. Fresh and distilled dioxane, methanol

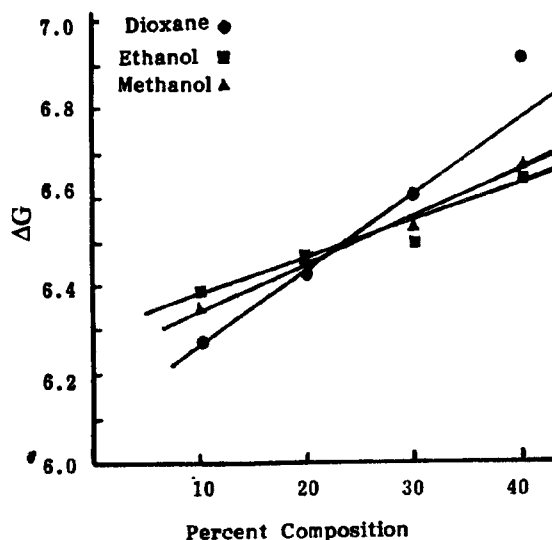


Fig. 8: Graph showing the variation in ΔG of benzoic acid in different concentration of dioxane, ethanol and methanol.

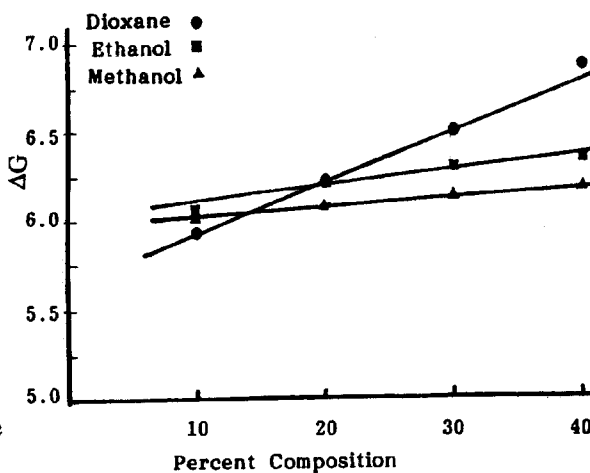


Fig. 9: Graph showing the variation in ΔG of sodium benzoate in different concentration of dioxane, ethanol and methanol.

and ethanol were used. Stock solution of 0.009 M benzoic acid in water and 0.1M sodium hydroxide containing 10, 20, 30 and 40% dioxane, methanol and ethanol were prepared. Stock solution of 0.01M sodium benzoate in water was also prepared. Sodium hydroxide solution was standardized with potassium hydrogen phthalate dried at 120°C by potentiometric method. The potentiometric titrations were performed in a thermostated double walled glass cell containing 50

ml of sample solution with sodium hydroxide. The pH was determined with Philips PW 9420 digital pH meter which was coupled with Ingold combined glass and reference electrode dipped in sample solution whose temperature was controlled by circulating water through the jacket of measuring cell, JULABO HC thermostated bath accurate to $\pm 0.1^\circ\text{C}$ was used for controlling the temperature. Prior to experiment the glass electrode was calibrated with 0.05 M potassium hydrogen phthalate (pH at $25^\circ\text{C} = 4.005$) and 0.01 M sodium tetraborate (pH at $25^\circ\text{C} = 9.18$) in respective organic-water mixture [3,17]. Sample solution was kept mixed by stirring with magnetic stirrer and inert by bubbling nitrogen gas which was dried and purified by passing through Fieser's solution [3] and distilled water in wash bottles. For dispensing titrant, Mettler burette DV-10 accurate to 0.01 ml was used.

The potentiometric measurements were performed on sample solution at different temperature and in different solvents and solvent composition.

The potentiometric data was analysed by a computer program written in GW-BASIC for calculation of dissociation constants of monobasic acid (benzoic acid) and monoacidic base (sodium benzoate)*.

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*Copy of the computer program can be obtained on request.