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STUDIES ON DISSOCIATION CONSTANT OF 3-BROMO-2-HYDROXY-5-METHYL ACETOPHENONE, ITS OXIME AND HYDRAZONE IN DIOXANE-WATER MIXTURES BY POTENTIOMETRY

The log k_I^H values of 3-bromo-2-hydroxy-5-methylacetophenone, its oxime and hydrazone in dioxane-water mixtures (20-75 (V/V)%) at various ionic strengths (0.01-0.1 M ($NaClO_4$)) and temperatures (20-40°C) have been determined potentiometrically. The role of solvents and ionic strengths on the dissociation constants has been discussed. The values of change in free energy, enthalpy and entropy have been calculated. The values of pK_m^H (minimum pK_I^H value at θ°C) have been calculated from Harned's equation. Three empirical equations have been employed to correlate dissociation constants with temperature.

1 — INTRODUCTION

The determination of log K_1 of 2-hydroxyacetophenone, its oxime and other substituted derivatives at various positions in the benzene ring has been the subject of many workers [1-5] in the recent years. In continuation of our earlier studies [5], the pH-metric measurement of the dissociation constants of 3-bromo-2-hydroxy-5-methylacetophenone (BHMA), its oxime (BHMAO) and hydrazone (BHMAH) by Irving and Rossotti's method [6] at different dioxane-water mixtures (ε), ionic strengths (μ) and temperatures are reported in this paper. The thermodynamic quantities: free energy change (Δ G), entropy (Δ S) and enthalpy (Δ H) for the compounds are evaluated. The pK_m^H (minimum pK_1^H value, at θ°C) has been calculated using Harned's equation. The acidity constants of the compounds are correlated with temperature using each of the following three empirical equations:

$$\log K = A + BT + CT^2 \qquad (1)$$

$$\log K = A/T + B + CT \qquad (2)$$

$$\log K = A/T + B \log T + C \qquad (3)$$

Attempts have been made to correlate the variation in the acid strength of these compounds with solvent and ionic strengths properties.

2 — EXPERIMENTAL

2.1 — *REAGENTS AND APPARATUS*

BHMA was synthesized by the acetylation of p-cresol with acetyl chloride and then 5-methyl phenyl acetate was treated with anhydrous $AlCl_3$ (1:3) for three hours at 120 °C. The product was treated with dilute HCl and 2-hydroxy-5-methyl acetophenone (m.p. 50 °C) was obtained. 2-hydroxy-5-methyl acetophenone was treated with 25% Br_2 solution in glacial acetic acid and kept overnight. The reaction mixture was poured into cold water, a yellow precipitate was obtained which was washed with water to remove excess of bromine, the product (BHMA) was crystallized from ethanol (m.p. 88 °C) [7]. The oxime (BHMAO) and hydrazone (BHMAH) were synthesized by usual procedure from BHMA using hydroxylamine hydrochloride and hydrazine hydrochloride respectively in the presence of anhydrous sodium acetate. The purity of the compounds was checked by elemental analysis and TLC.

Solutions of sodium hydroxide and perchloric acid B.D.H. (AnalaR) were prepared and standardized as usual. Sodium perchlorate (Riedel) was used to maintain the desired ionic strengths. Dioxane was purified as described by Vogel [8]. An inert atmosphere was maintained by bubbling nitrogen through the solution.

The pH measurements were done with systronic digital pH-meter type 335 (sensitivity 0.01 unit). The pH meter was calibrated at pH 4.00 and 9.18 with aqueous potassium hydrogen phthalate and borax buffers respectively.

The relation between pH-meter reading (B) in different percentage (V/V) dioxane-water mixtures and $[H^+]$ has been shown by Van Uitert and Haas [9] to be:

$$p^{H}corr. = -\log [H^+] = B + \log U_H$$

where the value of the correction factor, $\log U_H$ at a given composition of the medium at a fixed temperature can be obtained at any ionic strength from the expression:

$$\log U_H^{\circ} = \log U_H + \log \gamma\pm$$

where $\gamma\pm$ is the activity coefficient (mean) for the solvent composition and ionic strength for which U_H was determined.

The value of $\log U_H^{\circ}$ is reported to be independent of the ionic strength but is a function of temperature and dioxane-water composition. Recently, Rao and Mathur [10] gave an expression for the temperature dependence of $\log U_H^{\circ}$ for dioxane-water mixture.

$$\log U_H = (0.007406)t + 0.828 \qquad (4)$$

In the present work the value of $\log U_H$ was calculated from eq. (4) at 20°, 30° and 40°C which turned out to be 0.98, 1.05 and 1.12 respectively.

The value of $\log \gamma\pm$ was determined by interpolation of the plot of $\log 1/\gamma\pm$ vs. mean molality ($m\pm$) in dioxane-water mixtures at 30°C from the data given by Harned and Owen [11] for HCl.

2.2 — *PROCEDURE*

The experimental procedure of Irving and Rossotti [6] was used for potentiometric titrations of the following thermostated solutions under nitrogen atmosphere.

a) 2.0 ml $HClO_4$ (0.05M)
b) (a) + 5.0 ml ligand (0.01M)

against standard carbonate free sodium hydroxide (0.05 M). The ionic strengths 0.1 M, 0.05 M and 0.01 M were maintained by the addition of appropriate sodium perchlorate solution and keeping the total volume 40.0 ml. Such titrations were carried out in different dioxane-water mixtures.

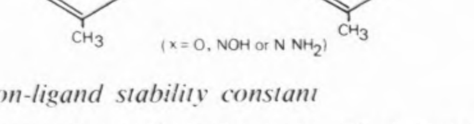
The mixing of dioxane with water is an exothermic reaction accompanied by a decrease in volume and hence it is necessary to correct the nominal volume ($V_{nom.}$) in the solvent medium employed in this study. The corret volume ($V_{corr.}$) at any temperature was calculated as Rao and Mathur [10]

$$V_{corr.} = V_{nom.}\ [0.x\ d_{H_2O} + (1-0.x)\ d_{dioxane}]\ \frac{1}{d_{mixture}}$$

where 0.x is the volumetric fraction of water. The data of density of water (d_{H_2O}), dioxane ($d_{dioxane}$) and mixture ($d_{mixture}$) given by Harned and Owen [11] were used.

2.3 — *CALCULATIONS*

The ligands behave as acids owing to the presence of a phenolic group. The dissociation of the ligands is shown as below:



Proton-ligand stability constant

The average number of protons (n_H) associated with ligand molecule is defined as:

$$\bar{n}_H = \frac{\text{total conc. of proton bound to ligand}}{\text{total conc. of ligand not bound to metal}}$$

To calculate the formation constant, n_H at different pH were calculated using the acid and ligand titration curves. The formula as by IRVING and ROSSOTTI [6] has been used:

$$\bar{n}_H = y - \frac{(V'' - V')(N^0 + E^0)}{(V^0 + V')T_{C_{L^0}}}$$

where V', V'' are the volume of alkali in acid and ligand titration to reach the same pH value. V^0, E^0 and N^0 are the total volume of the titrating mixture, total concentration of the acid and total concentration of the alkali respectively. T_{CL^0} is the total concentration of ligand and y is the number of dissociable protons.

The formation curves were obtained by plotting the graph between $\bar{n}_H$ and pH. The shape of the formation curve is as usual. The value of log K_1^H was calculated at $\bar{n}_H = 0.5$ and by least square method:

Table 1

log K_1^H values of the ligands at 30°C in 75% (V/V) dioxane-water mixtures at different ionic strengths ($NaClO_4$)

Ionic strengths	*BHMA*		*BHMAO*		*BHMAH*	
	Obs.	*Calc.*	*Obs.*	*Calc.*	*Obs.*	*Calc.*
0.10M	11.53	11.47	10.07	10.04	9.81	9.77
0.05M	11.70	11.65	10.25	10.22	9.98	9.95
0.01M	11.92	11.90	10.48	10.47	10.17	10.20
0.00*M	12.10	—	10.67	—	10.40	—

* By Extrapolation to zero ionic strength.

$$\log K_1^H = pH + \log \frac{\bar{n}_H}{1 - \bar{n}_H}$$

The values obtained from these methods were in good agreement. The average values of log K_1^H are reported at different μ, ε and temperature (Table 1, 2 and 3). The standard deviation [6] was found to be 0.030 ± 0.006.

3 — *RESULTS AND DISCUSSION*

Alkyl groups are electron-donating in character. Though the effect is quantitatively small, it is responsible for the increase in log K_1^H value. The methyl group present at 5-position in the benzene ring, destabilizes the phenoxide ion, due to its electron donating inductive effect as well as electron-repelling action

Table 2

log K_1^H values of the ligands at 30°C and $\mu = 0.1$ M ($NaClO_4$) in different dioxane-water mixtures

Dioxane (V/V) %	*Mole. fra. of dioxane*	*BHMA*	*BHMAO*	*BHMAH*
75	0.370	11.53	10.07	9.81
60	0.240	10.85	9.46	9.52
45	0.147	10.17	8.72	8.81
30	0.083	9.92	8.36	—
20	0.050	9.56	8.13	—
0*	0.000	9.35	7.95	8.15

* By Extrapolation to zero mole fraction of dioxane.

Table 3

log K_1^H and thermodynamic parameters at $\mu = 0.1$ M ($NaClO_4$), dioxane 75% (V/V) and different temperatures

Temp. (°K)	*pK_1^H (av.)*	*pK^H_m*	*θ (°C)*	*— ΔG (kcal mol⁻¹*	*— ΔH (kcal mol⁻¹) (av.)*	*ΔS (cal. deg⁻¹ mol⁻¹)*	*— ΔH* (kcal mol⁻¹)*
					BHMA		
293	11.68			15.68		35.90	5.744
303	11.53	10.59	166	16.01	5.167	35.79	5.722
313	11.37			16.31		35.60	5.657
					BHMAO		
293	10.22			13.72		28.25	5.272
303	10.07	9.93	154	13.98	5.448	28.17	5.217
313	9.96			14.29		28.24	5.118
					BHMAH		
293	9.88			13.27		29.37	4.761
303	9.81	9.12	141	13.62	5.612	29.57	4.670
313	9.66			13.86		29.38	4.535

* Using Harned's Equation.

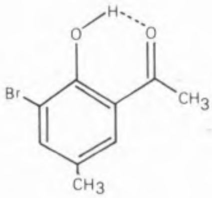
through conjugation effects. It also increase intramolecular hydrogen bonding between hydrogen of the phenolic 0H and oxygen of C = O group. On the other hand the introduction of an electronegative group (—Br) increases the acid strength of the parent compound.

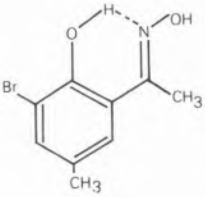
The log K_1^H value 11.85 for 2-hydroxy acetophenone (HA) was obtained in 75% dioxane at 30° C and $\mu = 0.1$ M ($NaClO_4$) by KAMAT and DATAR [2]. The log K_1^H value for BHMA was found to be 11.53 which is lower than 11.85, that may be due to the introduction of opposite nature groups in benzene ring i.e. $-CH_3$ and —Br groups at position 5 and 3 respectively.

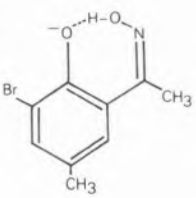
It is interesting to examine the influence of substitution of an oximino group for a keto oxygen. The value of log K_1^H for BHMAO is less than for BHMA. This may be due to the intramolecular hydrogen bond present in the system as follows:

(i) The O-H---N bond expected to be present in the neutral oxime molecule is weaker than the O-H---O bond of the corresponding BHMA. Consequently the release of the phenolic hydrogen of the oxime is facilitated.

(ii) Another acid strengthening factor may be due to the formation of oxime anion and hydrogen bond form as follows:







When the anion of an acid is stabilized by intramolecular hydrogen bond, there is a marked increase in the dissociation of the acid [13]. Although the hydrogen bonding in the case of oxime anion would be weak due to the infavourable ring size, but even then such a possibility does not exist in the case of the BHMA. The Same explanation may be given for lower value of log K_1^H for BHMAH.

Therefore the log K_1^H values for BHMAO and BHMAH were found to be lower i.e. 10.07 and 9.81 respectively.

3.1 — *EFFECT OF IONIC STRENGTH*

The formation curves ($\bar{n}_H$ *vs* pH) were drawn at different μ. There was no change in the shape of the curves, suggesting that various species coexist in the solution. The interaction of the ions decreases with the increase in the μ of the medium in which the reactions are studied. Hence an increase on μ corresponds to a decrease in log K_1^H value. The data was analysed by Bronsted equation:

$$\log K_1^H = \log K_1^{H^o} + A . \Delta Z^2 \sqrt{\mu}$$

where A is the Debye-Huckel constant, ΔZ^2 is the difference in the square of the charges of product and reactant ions and log $K_1^{H^o}$ is the formation constant at zero ionic strength. The values of log K_1^H were plotted against $\sqrt{\mu}$. It was found that log K_1^H was a linear function of $\sqrt{\mu}$ and can be represented by the equations:

$$\log K_1^H = 12.10 - 2.0\sqrt{\mu} \quad \text{for BHMA}$$
$$\log K_1^H = 10.67 - 2.0\sqrt{\mu} \quad \text{for BHMAO}$$
$$\log K_1^H = 10.35 - 2.0\sqrt{\mu} \quad \text{for BHMAH}$$

The experimental values of log K_1^H and those calculated (from above equations) show good agreement (Table 1).

3.2 — *EFFECT OF DIELECTRIC CONSTANT*

The degree of dissociation depends on the dielectric constant (ε) of the medium. A solvent of low ε increase the electrostatic force between the ions and facilitates the formation of molecular species resulting in an increase in log K_1 value [14]. The ε decreases-with an increase in dioxane percentage [15]. A linear relationship is observed when log K_1^H is plotted against mole fraction of dioxane-water mixture or $1/\varepsilon$ up to 45% (V/V) of dioxane. Deviations are observed at high percentage of dioxane. Slight improvement occurs when the activities of water are taken into consideration as suggested by YASUDA [16].

An approximate difference of log K_1^H values in mixed solvents can be obtained from BORN [17] equation:

$$\log {}_sK_1^H = \log {}_wK_1^H + 121.6 \left(\frac{1}{\varepsilon} - 0.0128\right) \left(\frac{1}{r_A} + \frac{1}{r_H}\right) \tag{5}$$

where r_A and r_H represent the radii of the acid anion and proton respectively. $\log {}_sK^H$ and $\log {}_wK_1^H$ are the formation constants of the ligands in solvent mixture and water respectively. The value of $r_H = 0.86$ A was used [18] and r_A was found to be 0.21, 0.21 and 0.30 A for BHMA, BHMAO and BHMAH respectively. These values are very low. That may be due to the (*i*) approximate nature of the Born equation (*ii*) solute-solvent interaction and solvent basicity of uncertain magnitude affecting the results.

3.3 — *EFFECT OF TEMPERATURE*

The ionization constant of a weak acid is a function of temperature and generally it has a maximum value near room temperature. An examination of the data given in Table 3 reveals that $\log K_1^H$ value of the ligands decrease as the temperature is raised.

The thermodynamic parameters free energy change (ΔG), enthalpy (ΔH) and entropy (ΔS) for the ionization of the ligands in 75% (V/V) dioxane-water medium at $\mu = 0.1$ M ($NaClO_4$) are calculated using usual equations:

$$\Delta G = -2.303\ RT \log K$$

$$\Delta H = 2.303\ R \frac{T_2 \times T_1}{T_2 - T_1} \log K''/K'$$

$$\Delta S = 2.303\ R \log K + \frac{\Delta H}{T}$$

where K'' and K' are the protonation constants at the absolute temperature T_2 and T_1 respectively.

The value of pK_m^H (minimum pK_1 value at θ°C) was calculated by Harned's equation [19]:

$$pK_1^H - pK_m^H = C(t-\theta)^2$$

$$\text{or } pK_1^H - Ct^2 = -2C\theta t + (pK_m^H + C\theta^2)$$

$$\text{where } C = \text{constant } (5.0 \times 10^{-5} \text{ degree}^{-2})$$

Thus the plot of $pK_1^H - Ct^2$ *vs* t should be a straight line with a slope of $-2C\theta$ and intercept $(pK_m^H + C\theta^2)$. The value of $pK_1^H - Ct^2$, for these ligands, were plotted against temperature 't' and it was observed that the linear plot is obtained. The value of θ and pK_m^H are reported in Table 3.

The value of ΔH was also calculated by Harned's equation [20]:

$$\Delta H = 2.303\ RT^2(t - \theta) \times 10^{-4}$$

and values are reported in Table 3.

Several empirical equations have been suggested to fit the variation in the acidity constants with temperature [21, 22]. The applicabillity of the equations (1-3 has been examined in correlating $\log K_1^H$ value of the ligands with temperature. The least square calculations were applied in evaluating the values of the coefficients of these equations. The values are reported in Table 4.

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Table 4
Acidity coefficients of the ligands

Compound	*Equation number*	*A*	*B*	*C*
BHMA	1	11.63605	0.0148	— 0.00005
	2	— 1389.3913	27.1164	— 0.0365
	3	— 345.66168	— 13.03	45.00344
	1	32.3708	— 0.1342	0.0002
BHMAO	2	5557.5654	— 22.6946	0.0476
	3	876.80038	— 3.53365	15.94466
	1	—23.5806	0.2314	— 0.0004
BHMAH	2	— 11115.1308	86.5502	— 0.1322
	3	— 2003.1517	— 20.38852	67.01127

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RESUMO

Determinaram-se os valores de pK_a da 3-bromo-2-hidroxi-5-metil-acetofenona e das respectivas oxima e hidrazona em misturas de dioxano e água (20-75% V/V a várias forças iónicas (0,01-0,1 M $NaClO_4$) e a várias temperaturas (20-40°C) pelo metodo potenciométrico.

Discute-se a influência dos solventes e das forças iónicas nas constantes de dissociação. Calcularam-se os valores de $\dot{\Delta} G$, ΔH e ΔS.

Os valores de pK_m^H (valor mínimo do pK_a, a temperatura θ °C foi calculada pela equação de Harned e utilizaram-se 3 equações empíricas para correlacionar as constantes de dissociação com a temperatura.