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Potentiometric Determination of the Apparent Dissociation Constants of Some Dicarboxylic Acids in Various Hydroorganic Media

Hassan A. Azab,*[†] Iman T. Ahmed,[‡] and Mohamed R. Mahmoud[§]

Department of Chemistry, Faculty of Science, Suez Canal University, Ismailia, Egypt, Department of Chemistry, Faculty of Science, Minia University, El-Minia, Egypt, and Department of Chemistry, Faculty of Science, Assiut University, Assiut, Egypt

The apparent dissociation constants of malic acid (hydroxybutanedioic acid), tartaric acid (2,3-dihydroxybutanedioic acid), phthalic acid (1,2-benzenedicarboxylic acid), and succinic acid (butane-1,4-dioic acid) were determined at 25 °C and ionic strength $I = 0.10$ mol dm^{-3} KNO_3 by potentiometric pH titration in pure water and water + methanol, water + ethanol, water + *N*,*N*-dimethylformamide, water + dimethyl sulfoxide, and water + acetonitrile. pK_a values increase with an increase in the concentration of the organic solvents. These results are discussed in terms of solvent characteristics. Solvent basicity and stabilization of the conjugate acid free base by hydrogen-bonding interactions in hydroorganic solvent media relative to pure aqueous media as well as proton−solvent interaction play an important role in the acid dissociation equilibrium.

Introduction

The determination of the apparent dissociation constants of an acid in mixtures of organic oxygen compounds with water provides useful results for the theoretical understanding of the ionization process in these media. Tartaric acid, malic acid, phthalic acid, and succinic acid and their alkali-metal salts have been of particular use as buffers for pH measurements in aqueous media as well as for pH* measurements in mixed solvents (Perrin and Dempsey, 1979). There have been extensive studies on the dissociation constants of acids in various mixed and nonaqueous solvents (Azab, 1992, 1993a,b; Azab et al., 1995; Benoit et al., 1991; Papanatasiou et al., 1984; Amira et al., 1987; Dash et al., 1987). In this paper we determined the apparent dissociation constants of the biologically important dicarboxylic acids, malic, tartaric, phthalic, and succinic, by potentiometric pH titrations in pure water and various water + methanol, water + ethanol, water + dimethylformamide, water + dimethyl sulfoxide, and water + acetonitrile mixtures containing different mass fractions of the organic solvent ranging between 0.0 and 0.55. The dependence of pK_a values on the composition of the solvent mixtures has been investigated in order to examine solute + solvent interactions.

Experimental Section

Chemicals. Malic acid (hydroxybutanedioic acid), tartaric acid (2,3-dihydroxybutanedioic acid), phthalic acid (1,2-benzenedicarboxylic acid), and succinic acid (butane-1,4-dioic acid) were BDH analytical grade and were further purified (Perin and Dempsey,1979). We also determined, by potentiometric pH titration, the molecular weights of these acids to verify/determine purity, especially for acidic/basic contaminants. The purity averaged 99.50% for all four compounds, with a standard deviation of 0.05%. The dried solvents used, methanol, ethanol, *N*,*N*-dimethylformamide, dimethyl sulfoxide, and acetonitrile, were of high purity (analytical reagent or spectro grade products). All solvents were used without further purification. Carbonate-free KOH was prepared and standardized by titration with standard potassium hydrogen phthalate. The molarity of HNO_3 was determined by titration with standard KOH solution. Generally, dilute solutions were prepared by appropriate dilution of the stock. The solvents were prepared by mixing weighed quantities of water and cosolvent.

Procedure. pH potentiometric measurements were made on solutions in a double-walled glass vessel at 25 ± 0.1 °C with a commercial Fischer combined electrode. The pH was measured with an Orion model 701A digital pH-meter (accurate to ±0.005 units). The instrument was standardized against standard buffers of pH 4.01 (phthalate buffer) and 9.20 (borate buffer). The instrument was rechecked after each experiment. The electrode system was calibrated in an aqueous medium in terms of hydrogen ion concentration instead of activities. Thus, all the constants determined in this work are concentration constants. Calibration of the electrode system was done by the MAGEC program (May et al., 1985) using the data of titration of nitric acid with potassium hydroxide, both of known concentration, under the same temperature and medium conditions. During the MAGEC calculation the $E°$ of the electrode system was determined in aqueous medium. Also the autoprotolysis constant of water, K_w, was refined. This refined K_w value is necessary as an adjustable parameter in pK_a calculation in pure water. The temperature was controlled by a Fischer Scientific Isotemp Refrigrated Circulator Model 9000 water thermostat, and it was maintained within ±0.1 deg. Purified nitrogen was bubbled through the solution to maintain an inert atmosphere. Efficient stirring of the solution was achieved with a magnetic stirrer. All test solutions (5×10^{-3} mol dm^{-3} carboxylic acid + 0.0127 mol dm^{-3} HNO_3) were prepared in a constant ionic medium, 0.1 mol dm^{-3} KNO_3, by mixing the appropriate amounts of dicarboxylic acids, nitric acid, potassium nitrate, and the proportion of the different organic solvents studied.

[†] Suez Canal University.
[‡] Minia University.
[§] Assiut University.

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Table 1. Refined pK_a* (Apparent Dissociation Constant) Values of Malic Acid in Different Mass Fractions w for wOrganic Solvent + (1 − w)Water Mixtures at (25.0 ± 0.1) °C and I = 0.10 mol dm^{-3} KNO$_3$

organic solvent	w	pK_{a1}* [a]	pK_{a2}* [a]
methanol	0.00	3.29 ± 0.03	4.73 ± 0.03
	0.20	3.64 ± 0.03	5.37 ± 0.04
	0.30		
	0.40	4.50 ± 0.04	6.39 ± 0.03
	0.55	5.01 ± 0.03	7.14 ± 0.04
ethanol	0.00	3.29 ± 0.03	4.73 ± 0.03
	0.20	3.58 ± 0.04	5.25 ± 0.03
	0.30		
	0.40	3.98 ± 0.04	5.41 ± 0.03
	0.55	4.45 ± 0.03	5.96 ± 0.03
DMF	0.00	3.29 ± 0.03	4.73 ± 0.03
	0.20	3.87 ± 0.04	5..41 ± 0.04
	0.30		
	0.40	4.38 ± 0.03	6.11 ± 0.04
	0.55	4.83 ± 0.03	6.60 ± 0.04
DMSO	0.00	3.29 ± 0.03	4.73 ± 0.03
	0.20	3.68 ± 0.03	5.17 ± 0.04
	0.30		
	0.40	4.10 ± 0.03	5.68 ± 0.04
	0.55	4.51 ± 0.03	6.30 ± 0.03
acetonitrile	0.00	3.29 ± 0.03	4.73 ± 0.03
	0.20	4.10 ± 0.03	5.80 ± 0.03
	0.30		
	0.40	4.89 ± 0.03	6.50 ± 0.04
	0.55	5.40 ± 0.03	6.81 ± 0.03

[a] pK_a* = corrected pK_a values according to Douhéret (1967, 1968) ± uncertainties (refer to statistically determined uncertainities at small 95% confidence intervals).

Table 2. Refined pK_a* (Apparent Dissociation Constant) Values of Tartaric Acid in Different Mass Fractions w for wOrganic Solvent + (1 − w)Water Mixtures at (25.0 ± 0.1) °C and I = 0.10 mol dm^{-3} KNO$_3$

organic solvent	w	pK_{a1}* [a]	pK_{a2}* [a]
methanol	0.00	2.90 ± 0.03	4.10 ± 0.03
	0.20	3.18 ± 0.03	4.59 ± 0.03
	0.30	3.59 ± 0.03	4.79 ± 0.04
	0.40	3.80 ± 0.04	5.19 ± 0.02
	0.55		
ethanol	0.00	2.90 ± 0.03	4.10 ± 0.03
	0.20	3.00 ± 0.03	4.49 ± 0.03
	0.30	3.49 ± 0.04	4.59 ± 0.03
	0.40		
	0.55		
DMF	0.00	2.90 ± 0.03	4.10 ± 0.03
	0.20	3.43 ± 0.04	4.89 ± 0.03
	0.30		
	0.40	4.05 ± 0.03	5.29 ± 0.03
	0.55		
DMSO	0.00	2.90 ± 0.03	4.10 ± 0.03
	0.20	3.29 ± 0.03	4.86 ± 0.03
	0.30		
	0.40	3.79 ± 0.03	5.10 ± 0.04
	0.55	4.10 ± 0.03	5.38 ± 0.03
acetonitrile	0.00	2.90 ± 0.03	4.10 ± 0.03
	0.20	3.69 ± 0.03	4.82 ± 0.04
	0.30		
	0.40	3.98 ± 0.03	5.21 ± 0.04
	0.55	4.10 ± 0.03	5.38 ± 0.03

[a] pK_a* = corrected pK_a values according to Douhéret (1967, 1968) ±uncertainties (refer to statistically determined uncertainties at small 95% confidence intervals).

The concentration of hydrogen ion was decreased by the addition of potassium hydroxide, prepared in the same medium used for the test solution. At each mixture, at least 6 titrations (35 measurements each) were performed. The concentration of free hydrogen ion, C_{H^+}, at each point of the titration was calculated from the measured electromotive force (emf), E, of the cell RE/TS/GE (RE and GE denote the reference and glass electrodes, respectively, and TS is the test solution) using the Nernst equation

$$E = E° + Q \log C_{H^+} \tag{1}$$

where $E°$ is a constant that includes the standard potential of the glass electrode. It is to be assumed that the activity coefficient is constant, an assumption usually justified by performing the experiments with a medium of high ionic strength (0.1 mol dm^{-3} KNO$_3$). Values for K_w for water in water + organic solvent systems have been taken from the literature (Bates, 1964; Woolley et al., 1970; Woolley and Hepler, 1972; Gutbezahl et al., 1953; Harned et al., 1939).

The pH-meter readings have been corrected in accordance with the method described by Douhéret (1967, 1968). This was carried out to account for the difference in basicity, relative permittivity, and ion activity in partially aqueous solutions relative to pure solvent. The protonation constants were then determined by use of the Bjerrum function (Bjerrum, 1921)

$$\bar{n} = H_T - h + (K_w/h)/A_T = \beta_1 h + 2\beta_2 h^2/1 + \beta_1 h + \beta_2 h^2 \tag{2}$$

which is calculated from the experimental quantities, h, the total concentrations of titratable hydrogen ion H_T, and the total reagent concentration A_T. The pK_a values were determined from the overall protonation constants β_1 and β_2 calculated by the linearization method of Irving and Rossotti (1953). Initial estimates of pK_a values were refined with the ESAB2M computer program (De Stefano et al., 1987) by minimizing the error squares sum:

$$U_v = \sum_i W_i(V_i - V_{calcd,i})^2 \tag{3}$$

where V_i and $V_{calcd,i}$ are experimental and calculated volumes of the titrant for every point i of the titration curve. The weight is calculated by

$$1/W_i = S_i^{\,2} = S_V^{\,2} + (\delta V_i/\delta E_i)^2 S_E^{\,2} \tag{4}$$

where S_i, S_V, and S_E are estimated variance and estimates of standard deviation in titrant volume and potential, respectively. Titrant volume, $V_{calcd,i}$, can be calculated from an explicit equation (Arena et al., 1979). The program ESAB2M minimizes eq 3 by using the Gauss−Neuton nonlinear least-squares method (Dixon, 1972). Our calculation has been performed with a Gaussian error in V of S_V = 0.005. In our potentiometric pH titrations we put $E°$ = 0 (formal potential of the electrodic couple) in the input instructions, since the program reads in pH in this case.

Results and Discussion

The pK_a values of malic, tartaric, phthalic, and succinic acids in different solvent mixtures are given in Tables 1−4. The calculated pK_a values of the dicarboxylic acids studied in pure water agree well with the literature values (Perrin and Dempsey, 1979).

Effect of the Amphiprotic Solvents. Consider an acid HA at molality m in mixed amphiprotic solvent (SH). It is assumed that the permittivity of the mixed solvent is sufficiently large to permit a certain amount of ionization. The proton activity a_H, as a measure of acidity, can be expressed (Bates, 1964) in terms of K_{HA} and K_{SH}, which are, respectively, the acidity constants of HA and SH$_2^+$:

$$a_H = [mK_{HA}K_{SH}\gamma_{SH_2^+}\gamma_{HA}/\gamma_{SH}\gamma_{A^-}]^{1/2} \tag{5}$$

Table 3. Refined pK_a* (Apparent Dissociation Constant) Values of Succinic Acid in Different Mass Fractions w for wOrganic Solvent + (1 − w) Water Mixtures at (25.0 ± 0.1) °C and I = 0.10 mol dm^{-3} KNO$_3$

organic solvent	w	pK_{a1}* [a]	pK_{a2}* [a]
methanol	0.00	4.03 ± 0.03	5.28 ± 0.03
	0.20	4.58 ± 0.03	5.96 ± 0.03
	0.30		
	0.40	5.08 ± 0.04	6.57 ± 0.04
	0.55	5.58 ± 0.03	7.21 ± 0.03
ethanol	0.00	4.03 ± 0.03	5.28 ± 0.03
	0.20	4.50 ± 0.03	5.87 ± 0.03
	0.30		
	0.40	5.01 ± 0.04	6.52± 0.03
	0.55	5.41 ± 0.03	6.87 ± 0.03
DMF	0.00	4.03 ± 0.03	5.28 ± 0.03
	0.20	4.66 ± 0.04	6.19 ± 0.03
	0.30		
	0.40	5.29 ± 0.03	6.78 ± 0.03
	0.55	5.80 ± 0.04	7.36 ± 0.03
DMSO	0.00	4.03 ± 0.03	5.28 ± 0.03
	0.20	4.33 ± 0.03	5.78 ± 0.04
	0.30		
	0.40	5.17 ± 0.03	6.64 ± 0.03
	0.55	5.64 ± 0.04	6.99 ± 0.04
acetonitrile	0.00	4.03 ± 0.03	5.28 ± 0.03
	0.20	5.18 ± 0.04	6.79 ± 0.04
	0.30		
	0.40	5.73 ± 0.04	7.20 ± 0.03
	0.55	6.39 ± 0.04	8.11 ± 0.03

[a] pK_a* = corrected pK_a values according to Douhéret (1967, 1968) ± uncertainties (refer to statistically determined uncertainties at small 95% confidence intervals).

Table 4. Refined pK_a* (Apparent Dissociation Constant) Values of Phthalic Acid in Different Mass Fractions w for wOrganic Solvent + (1 − w)Water Mixtures at (25.0 ± 0.1) °C and I = 0.10 mol dm^{-3} KNO$_3$

organic solvent	w	pK_{a1}* [a]	pK_{a2}* [a]
methanol	0.00	2.95 ± 0.03	5.42 ± 0.03
	0.20	3.30 ± 0.04	5.70 ± 0.03
	0.30		
	0.40	3.60 ± 0.04	6.50 ± 0.03
	0.55	3.90 ± 0.03	6.74 ± 0.04
ethanol	0.00	2.95 ± 0.03	5.42 ± 0.03
	0.20	3.20 ± 0.03	5.60 ± 0.04
	0.30		
	0.40	3.41 ± 0.03	6.40 ± 0.03
	0.55	3.70 ± 0.04	6.81 ± 0.03
DMF	0.00	2.95 ± 0.03	5.42 ± 0.03
	0.20	3.40 ± 0.03	5.90 ± 0.03
	0.30		
	0.40	3.90 ± 0.03	6.05 ± 0.03
	0.55	4.20 ± 0.03	6.35 ± 0.04
DMSO	0.00	2.95 ± 0.03	5.42 ± 0.03
	0.20	3.10 ± 0.03	5.50 ± 0.04
	0.30		
	0.40	3.31 ± 0.04	6.11 ± 0.03
	0.55	3.90 ± 0.03	6.47 ± 0.03

[a] pK_a* = corrected pK_a values according to Douhéret (1967, 1968) ± uncertainties (refer to statistically determined uncertainties at small 95% confidence intervals).

where $\gamma_{SH_2^+}$, γ_{HA}, γ_{SH}, and γ_A- are the activity coefficients of the species SH$_2^+$, HA, SH, and A$^-$, respectively. The same treatment may be applied for the dissociation of an acid H$_2$A in a mixed amphiprotic solvent (SH), where eq 5 can apply for the equilibrium

$$\mathrm{HA^- \rightleftharpoons A^{2-} + H^+}$$

$$K_{HA^-} = a_{H^+} m_A{}^{2-} \gamma_A{}^{2-} / m_{HA^-} \gamma_{HA^-} \qquad (6)$$

A decrease in the permittivity usually causes $\gamma_{SH_2^+}/\gamma_{SH}$ and γ_A-/γ_{HA} to increase, and it is possible that both of these ratios will increase by about the same amount (Hammett, 1928). Hence, a lowering of the permittivity due to addition of the methanol or ethanol may have little effect on the acidity of an unbuffered solution of malic, tartaric, phthalic, or succinic acid. The autoprotolysis constant of water is slightly influenced by addition of methanol or ethanol (the pK_a of water changes from 14.0 to 14.90 for a 0.50 mass fraction ethanol + water mixture (HA + SH $\rightleftharpoons$ SH$_2^+$ + A$^-$). Thus, changing the medium basicity by addition of methanol or ethanol may result in a relatively low stabilization of the conjugate base of the dicarboxylic acids studied compared to that in a pure aqueous medium, thereby causing an increase in the pK_a value.

Effect of Dipolar Aprotic Solvents (N,N-Dimethylformamide and Dimethyl Sulfoxide). The observed increase in the pK_a values of the different dicarboxylic acids studied as the solvent is enriched in the dipolar aprotic solvent dimethylformamide or dimethyl sulfoxide can mainly be attributed to expected low stabilization of the conjugate free base of malic, tartaric, phthalic, and succinic acids by a hydrogen bond donated from solvent molecules in dimethylformamide or dimethyl sulfoxide + water mixtures compared to that obtained in a pure aqueous medium. This in turn results in a high pK_a value.

Effect of a Low Basic Aprotic Acetonitrile Solvent. The presence of acetonitrile as coorganic solvent exerts a pronounced effect on the pK_a values of malic, tartaric, phthalic, and succinic acids as compared to the effect of the other coorganic solvents studied (methanol, ethanol, dimethylformamide, and dimethyl sulfoxide). This behavior can be mainly attributed to the following effects.

(i) Solute−Solvent Interaction Effect. Acetonitrile is considered to be both a poorer acceptor as well as donor of hydrogen bonds compared to water. Thus, one may expect a low stabilization of the free conjugate bases of the dicarboxylic acids studied by hydrogen-bonding interactions in the presence of this coorganic solvent. This leads to a higher pK_a value in such media in comparison to that obtained in pure aqueous solution.

(ii) Proton−Solvent Interaction Effect. Since acetonitrile is a weakly basic solvent, one must expect that the H$^+$ ion becomes less stabilized in the presence of this coorganic solvent due to hydrogen ion−solvent interaction (Bates, 1969).

Thus, increasing the acetonitrile proportion in the aqueous medium results in a high activity coefficient of the proton, i.e., a high pK_a value.

According to Bates (1964) solvent effects on the dissociation equilibria of the dicarboxylic acids under investigation can be expressed by eq 7, where $\bar{r}$ is the common radius of

$$\mathrm{p}K_a{}^* - \mathrm{p}K_a = 121.6n/\bar{r}(1/\epsilon_2 - 0.0128) \qquad (7)$$

all the ions, ϵ_2 is the relative permittivity of the mixed organic solvent, n = 2 for HA,A pairs of the charge type A°B$^-$, n = 4 for the charge type A$^-$B^{2-}, and n = 0 for the charge type A$^+$B°, while 0.0128 is the reciprocal of the permittivity of water at 25 °C. The pK_a for dicarboxylic acids as might be expected from eq 7 does indeed increase markedly as the relative permittivity decreases. Thus, the properties of solvents such as relative permittivity (electrostatic effect) and acidic or basic strength play a major but not an exclusive role in the protonation of the diffferent acids investigated. It must be stated that eq 7, in the present form, is valid only at 25 °C.

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