Acid−Base Dissociation Constants of *o*-Phthalic Acid in Acetonitrile/Water Mixtures over the (15 to 50) °C Temperature Range and Related Thermodynamic Quantities

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Potassium hydrogen phthalate (KHP) is a primary titrimetric standard, and KHP solutions are also used as standards for pH reference values, in pure water or in hydrorganic solvent mixtures. However, the pH of these solutions can be affected by any shift in the pK_{a1} or pK_{a2} of the substance due to changes in the solvent composition or temperature. In this work, the two dissociation constants of *o*-phthalic acid were independently determined for different compositions of acetonitrile/water mixtures within the range from 0 % to 70 % by weight, in steps of 10 %, and at different temperatures from (15 to 50) °C, in steps of 5 °C. The dependence of ln K_a on the inverse of temperature has been examined by using statistical methods, and the corresponding ionization thermodynamic functions have been calculated for different acetonitrile compositions.

Introduction

Potassium hydrogen phthalate (KHP) is an important standard substance in solution chemistry. It is used as a titrimetric primary standard, and also its solutions provide reference pH values. To be more precise, solutions of 0.05 m KHP give the pH reference standard value, pH_{RVS}, for the calibration of any type of pH electrode.[1−3] It is especially recommended for solutions prepared in polar solvent mixtures.[3] However, this recommendation should be endorsed by the knowledge of the variability that physical and chemical conditions can introduce to the referenced pH value and buffer capacity of the solution.

Several authors have reported previously the variation of the pH of KHP solutions with temperature and solvent composition.[4−8] However, KHP solutions are not the typical buffer solutions where the pH is buffered near the pK_a value. In these particular kinds of solution, the pH is an intermediate value that lies between pK_{a1} and pK_{a2}. The consequences are two: on one hand, a shift in any of its dissociation constants leads directly to a change in the pH value of the solution, but on the other, to know the behavior of the pH with the solvent composition and temperature does not provide knowledge about the effect of these variables on the dissociation equilibria. The effects observed for any particular solution cannot be extended to other solvent mixtures or conditions.

There are some studies showing the effect of temperature on the pK_a of *o*-phthalic acid,[9−12] and also the effect of solvent on the pK_a of *o*-phthalic acid.[8,13,14] However, these works do not study the combined effect, e. g., the dissociation enthalpies at high organic solvent compositions are usually quite different from those reported in pure water.[15] Therefore, a systematic study of the effects of temperature and solvent composition on the pK_{a1} and pK_{a2} of *o*-phthalic acid is required and this is the aim of this work.

Conductometric methods or potentiometric methods using hydrogen gas electrodes are used to measure pH and to determine pK_a values with high precision, typically of about ± 0.002 logarithmic units.[1,3,16] However, these determinations are quite tedious and are not suitable for carrying out a systematic study in a reasonable time. Another option is to use a glass combination electrode. Although this potentiometric method is not so rigorous as other methods, it allows systematic measurements varying both, simultaneously, temperature and solvent mixture composition. These electrodes are selective to hydrogen ions and allow the measurement of the pH by single immersion, but its use has two drawbacks. First, the combination electrode involves the use of a 3 M KCl salt bridge between the internal reference and the external solution. This salt bridge reduces the junction potential, but it does not become zero.[17−19] This potential varies from one solution to another, and this variability increases the uncertainty of the measured pH with respect to that obtained by the other methods. For this reason, the reported accuracy cannot be better than ± 0.02 pH/pK_a units. This accuracy can be achieved when the calibration is carried out following the multipoint calibration method using three or more pH standard solutions.[20] Second, when measuring pH in solvent mixtures with a glass combination electrode calibrated in pure water, it is necessary to correct the pH scale. For the case of acetonitrile/water mixtures at different temperatures, the δ-parameter required to convert the ${}_{w}^{s}pH$ into ${}_{s}^{s}pH$ has been previously determined.[21,22] It should be noticed here that both pH scales, ${}_{w}^{s}pH$ and ${}_{s}^{s}pH$, refer to the pH measurements in the organic solvent/water mixtures. In the first case, the standard state chosen for the proton is infinite dilution of the hydrogen ion in water, whereas in the second case, it is the infinite dilution of the hydrogen ion in the same solvent where the measurement is made. This means, in practical work, that in the first case the electrode system is standardized with ordinary aqueous buffers, but in the second one the standardization is performed with buffers prepared in the same solvent of the solution to be measured. Thus, lowercase left-hand superscripts indicate the

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solvent, water (w) or nonaqueous, or mixed solvent (s) in which measurements are being made; lowercase left-hand subscripts indicate the solvent in which the ionic activity coefficient γ is referred to unity at infinite dilution (w or s).[2,23] The relationship between both operational pH scales is the δ parameter that includes the "medium effect", which is related to the energy required to transfer the infinite diluted hydrogen ion between the solvent (s) and pure water (w), and the junction potential due to the electrode system. Thus, the δ quantity depends not only on the solvent and temperature of the measured solution but also on the combination electrode used in the measurements. However, it has been demonstrated that modern combination glass electrodes filled with 3 M KCl show the same junction potential for measurements in acetonitrile/water mixtures in a wide temperature range. Thus, previously published δ values[21] are only dependent on the temperature and composition of the binary solvent of the solution to be measured, and they are used in this study.

In this work, we determine pK_{a1} and pK_{a2} of *o*-phthalic acid at different temperatures and solvent composition in acetonitrile/water binary mixtures, evaluating the independent and combined effect of these variables on both pK_a values. Solutions of known analytical concentrations of the associated and dissociated forms of *o*-phthalic acid have been prepared at every solvent mixture composition. The pH values of these solutions have been carefully measured and the corresponding pK_a calculated. Finally, the dependence of $\ln K_a$ on the inverse of temperature has been examined by using statistical methods, and the corresponding ionization thermodynamic functions have been calculated. Changes in enthalpy of ionization for the first ionization equilibrium are independent of temperature over all the compositions. However, temperature dependence of change in enthalpies for the second ionization reaction can be calculated by using the Clarke and Glew thermodynamic approach.

Experimental Section

Instrumentation. ${}_{w}^{s}$pH values of solutions were measured with a RossUltra 8102SC electrode connected to a Crison micropH 2002 potentiometer. Thermostating of pH standard buffers and solutions was performed with a Selecta Tectron 3473100 water bath ($\pm$ 0.1 °C). Titrations of hydrochloric and sodium hydroxide solutions were carried out using a Metrohm Dosimat 665 Autoburet.

Chemicals. Solvents were prepared using water provided by a Milli-Q purification system, and acetonitrile was Merck HPLC grade. Other chemical reagents were analytical grade or better. Calibrations of the combined pH electrode were performed with the commercial aqueous standard solutions: Crison ${}_{w}^{w}$pH$^{20°C}$ = 7.00, Crison ${}_{w}^{w}$pH$^{20°C}$ = 4.01, and Panreac ${}_{w}^{w}$pH$^{20°C}$ = 2.00.

Procedures. For every dissociation constant to be studied, five different solutions were prepared at a given acetonitrile/water composition. The studied composition ranges were from (0 to 70) % (w/w) in steps of 10 %. Dissociation ratios between acid and basic species in each solution varied within the range from 0.4 to 0.6. To prepare each solution, approximately 510 mg of KHP was weighted followed by the accurate volume addition of either hydrochloric acid or potassium hydroxide solution, depending on the studied pK_a. The required quantities were calculated according to the exact weight of KHP. Finally, known masses of pure water and pure acetonitrile were added to complete 50 g of total solvent with the desired composition and a KHP analytical concentration of 0.05 m. The ionic strength varied depending on the dissociation ratio and the equilibrium studied (first or second). It resulted in a set of 40 solutions for

the determination of the first dissociation constant and another set of 40 solutions for the study of the second dissociation constant. The hydrochloric acid and potassium hydroxide solutions were prepared and standardized against dried trishydroxymethylaminomethane or potassium hydrogen phthalate, respectively, following standard procedures. All quantities, even the acetonitrile addition, were measured by weight to ensure a precision of $\pm$ 0.01 % or better. All the solutions, including the calibration standards and the solutions to be measured, as well as the used pH electrode, were thermostatted at each temperature (from (15 to 50) °C) over 45 min before starting the measurements. A multipoint calibration procedure with three thermostatted standard buffer solutions was used for the electrode calibrations.[14] The glass electrodes were immersed into the solutions through a holed cap, and the solutions were frequently shaken to avoid changes in solvent compositions by condensation into the internal flask walls. This caution is important to minimize errors due to the known effect that solvent composition has on the dissociation constants. The calibration procedure was repeated every five measurements to minimize drifts; calibration was followed by sequential measurement of pH of the solutions with different acetonitrile composition. Hence, the pH values of the five solutions corresponding to a unique solvent composition were based on five different calibration procedures.

All necessary cautions were taken into account for solvent and reagent handling. Chemical waste was disposed for a proper residual treatment.

Data Treatment. The first dissociation constant of *o*-phthalic acid can be obtained from the following expression

$$
{}_{s}^{s}pK_{a1} = -\log\left(\frac{m_{HPh^-} + m_{H^+}}{m_{H_2Ph} - m_{H^+}}\right) - \log {}_{s}^{s}\gamma_{HPh^-} + {}_{s}^{s}pH_m
$$

(1)

where m is molal analytical concentrations and the lowercase right-side subscript indicates the chemical species: HPh$^-$, hydrogen phthalate; H$_2$Ph, *o*-phthalic acid; and H$^+$, hydrogen ion. ${}_{s}^{s}\gamma_{HPh^-}$ and ${}_{s}^{s}pH_m$ are the activity coefficients of the hydrogen phthalate ion and the pH in the molality scale, respectively. The activity coefficient of the neutral molecule was assigned a value of unity, as customary. The molal standard state of all the species is referred to infinite dilution in the same solvent and temperature. In the last expression, the activity coefficient of hydrogen phthalate is estimated through the Debye−Hückel equation

$$
-\log {}_{s}^{s}\gamma = \frac{Az^2\sqrt{I}}{1 + a_0B\sqrt{I}}
$$

(2)

where I stands for the ionic strength in the molal scale; z is the charge of the ionic species; and A and a_0B are parameters of the equation which can be calculated by assuming the Bates−Guggenheim convention

$$
A = 1834600\frac{\sqrt{\rho_s}}{(\varepsilon_s T)^{3/2}}
$$

(3)

$$
a_0B = 1.5\sqrt{\left(\frac{\varepsilon_w}{\varepsilon_s}\right)\left(\frac{\rho_s}{\rho_w}\right)}
$$

(4)

T is the temperature in absolute scale; ε indicates the static dielectric constants; ρ is densities, all of them at a given temperature; and subscripts w and s indicate pure water and solvent (or solvent mixture), respectively.[22] Considerations and limitations of this theory have been fairly explained.[16,23,24] The

Table 1. First Dissociation Constant of *o*-Phthalic Acid at Different Temperatures and Acetonitrile Compositions in the Standard State of the Same Solvent and Molal Concentrations ($_s^s pK_1$)^a

ACN % (w/w)	15 °C	20 °C	25 °C	30 °C	35 °C	40 °C	45 °C	50 °C
0	2.93_5 (± 0.007)	2.93_8 (± 0.004)	2.94_8 (± 0.002)	2.94_4 (± 0.003)	2.95_5 (± 0.004)	2.95_6 (± 0.004)	2.97_0 (± 0.011)	2.97_4 (± 0.006)
10	3.20_1 (± 0.007)	3.19_8 (± 0.004)	3.20_1 (± 0.004)	3.19_0 (± 0.005)	3.19_3 (± 0.004)	3.18_4 (± 0.007)	3.18_7 (± 0.017)	3.18_4 (± 0.007)
20	3.45_6 (± 0.006)	3.44_5 (± 0.005)	3.43_6 (± 0.003)	3.41_8 (± 0.005)	3.41_1 (± 0.005)	3.39_5 (± 0.008)	3.39_1 (± 0.015)	3.38_5 (± 0.005)
30	3.69_0 (± 0.008)	3.67_0 (± 0.004)	3.65_5 (± 0.004)	3.63_3 (± 0.004)	3.62_0 (± 0.005)	3.59_7 (± 0.010)	3.58_9 (± 0.014)	3.57_9 (± 0.006)
40	3.91_6 (± 0.007)	3.89_1 (± 0.006)	3.87_2 (± 0.008)	3.84_7 (± 0.006)	3.82_8 (± 0.005)	3.80_9 (± 0.008)	3.80_0 (± 0.009)	3.78_2 (± 0.011)
50	4.14_5 (± 0.009)	4.12_0 (± 0.007)	4.09_6 (± 0.009)	4.07_1 (± 0.006)	4.05_4 (± 0.009)	4.03_0 (± 0.009)	4.01_6 (± 0.009)	4.00_1 (± 0.011)
60	4.41_0 (± 0.008)	4.37_8 (± 0.005)	4.35_7 (± 0.009)	4.33_5 (± 0.009)	4.31_6 (± 0.010)	4.29_4 (± 0.010)	4.28_4 (± 0.015)	4.26_9 (± 0.016)
70	4.76_1 (± 0.009)	4.73_5 (± 0.010)	4.70_3 (± 0.009)	4.67_6 (± 0.007)	4.65_7 (± 0.006)	4.63_6 (± 0.009)	4.62_8 (± 0.013)	4.61_2 (± 0.014)

^{a} The standard deviations of pK_a values are of ± 0.02. In parentheses, the standard deviation of the averaged pK_a value obtained from different solutions.

Table 2. Second Dissociation Constant of *o*-Phthalic Acid at Different Temperatures and Acetonitrile Compositions in the Standard State of the Same Solvent and Molal Concentrations ($_s^s pK_2$)^a

ACN % (w/w)	15 °C	20 °C	25 °C	30 °C	35 °C	40 °C	45 °C	50 °C
0	5.38_8 (± 0.005)	5.39_1 (± 0.007)	5.39_5 (± 0.004)	5.40_4 (± 0.003)	5.41_1 (± 0.003)	5.42_8 (± 0.006)	5.44_5 (± 0.001)	5.46_0 (± 0.006)
10	5.81_3 (± 0.005)	5.83_1 (± 0.004)	5.84_7 (± 0.002)	5.86_5 (± 0.003)	5.88_1 (± 0.004)	5.90_0 (± 0.005)	5.92_3 (± 0.002)	5.94_1 (± 0.009)
20	6.34_7 (± 0.007)	6.36_3 (± 0.005)	6.37_5 (± 0.005)	6.39_2 (± 0.004)	6.40_7 (± 0.003)	6.41_9 (± 0.006)	6.43_7 (± 0.006)	6.45_0 (± 0.006)
30	6.84_3 (± 0.007)	6.85_8 (± 0.004)	6.86_5 (± 0.002)	6.87_9 (± 0.006)	6.88_6 (± 0.005)	6.89_8 (± 0.007)	6.91_3 (± 0.006)	6.92_9 (± 0.008)
40	7.26_2 (± 0.012)	7.26_9 (± 0.004)	7.28_3 (± 0.002)	7.30_2 (± 0.002)	7.32_1 (± 0.005)	7.33_3 (± 0.008)	7.34_7 (± 0.006)	7.36_6 (± 0.009)
50	7.63_2 (± 0.009)	7.64_9 (± 0.007)	7.67_3 (± 0.004)	7.70_3 (± 0.003)	7.73_2 (± 0.004)	7.74_8 (± 0.006)	7.76_8 (± 0.004)	7.79_1 (± 0.007)
60	8.02_2 (± 0.004)	8.05_9 (± 0.007)	8.09_5 (± 0.003)	8.13_6 (± 0.002)	8.17_4 (± 0.006)	8.20_1 (± 0.008)	8.23_3 (± 0.009)	8.25_5 (± 0.015)
70	8.46_3* (± 0.032)	8.55_1* (± 0.023)	8.60_4 (± 0.017)	8.66_1 (± 0.008)	8.71_9 (± 0.004)	8.75_8 (± 0.004)	8.80_3 (± 0.009)	8.84_2 (± 0.016)

^{a} The standard deviations of pK_a values are of ± 0.03 excepting that indicated with *. In parentheses the standard deviation of the averaged pK_a value obtained from different solutions. * Standard deviation is ± 0.04.

Table 3. Comparison of pK_a Values for the First and Second Dissociation of *o*-Phthalic Acid in Water with Those Reported in the Literature

	temperature (°C)							
	15	20	25	30	35	40	45	50
pK_{a1}	2.935^a	2.938	2.948	2.944	2.955	2.956	2.970	2.974
	2.933^b	2.940	2.948	2.957	2.967	2.978	2.986	2.997
	2.937^c	2.943	2.950	2.958	2.967	2.978	2.988	3.001
pK_{a2}	5.388^a	5.391	5.395	5.404	5.411	5.428	5.445	5.460
	5.396^d	5.396	5.399	5.407	5.418	5.434	5.452	5.475
	5.405^e	5.405	5.408	5.415	5.427	5.442	5.462	5.485

^{a} This row shows the values measured in this study. ^{b} This row shows the values taken from ref 12. ^{c} This row shows the values taken from ref 9. ^{d} This row shows the values taken from ref 11. ^{e} This row shows the values taken from ref 10.

$_s^s pH_m$ values are calculated by converting the experimental $_w^s pH$ of the solutions and using the δ_m conversion parameter as

$$_s^s pH_m = {}_w^s pH - \delta_m \tag{5}$$

The δ_m parameter at each temperature and composition has been taken from the literature.[21]

The second dissociation constant, $_s^s K_2$, is obtained after measuring the $_w^s pH$ values of the second set of solutions, then converting it to $_s^s pH_m$ with the corresponding δ_m parameter and finally calculated from the following expression

$$_s^s pK_{a2} = -\log\left(\frac{m_{Ph^{2-}} + m_{H^+}}{m_{HPh^-} - m_{H^+}}\right) - \log\left(\frac{_s^s \gamma_{Ph^{2-}}}{_s^s \gamma_{HPh^-}}\right) + {}_s^s pH_m \tag{6}$$

The notation follows the same criteria as used in eq 1, thus the lowercase subscript Ph^{2-} indicates phthalate ions, and all quantities here correspond to the set of solutions prepared for measuring the second dissociation equilibrium.

Results and Discussion

Results for the first and second dissociation constants with the standard states referred to species in the molal scale at each solvent composition and temperature are shown in Tables 1 and

2, respectively. The standard deviation of each $_s^s pK_a$ value is calculated applying the standard propagation rules to the three main contributions: the standard deviation between values obtained from the different solutions (see them in parentheses in Tables 1 and 2), the standard deviation of the δ_m parameter required to convert the measured $_w^s pH$ into $_s^s pH$ which was reported as ± 0.023 logarithmic units for solutions with acetonitrile compositions between (0 to 75) % (w/w),[21] and the uncertainty due to the liquid junction potential considered to be ± 0.02. The resulting standard deviation for the reported $_s^s pK_a$ values are ± 0.03 for almost all values excepting two where the experimental conditions (higher acetonitrile composition and lower temperature) raise the standard deviation up to ± 0.04. Thus, the precision of these pK_a values is quite good for potentiometric measurements in solvent mixtures. In Table 3, experimental pK_a values in pure water are compared with those compiled from the literature. Values obtained in this work for the first and second dissociation constant are in quite good agreement with those reported by other authors.[9−12]

Rondinini and Nesse have measured the potential of a cell containing potassium hydrogen phthalate and proposed three equations to estimate pK_{a1} values at three temperatures, (15, 25, and 35) °C, and at any acetonitrile composition.[25] The calculated pK_{a1} values are compared with data measured in this study in Table 4. They are in good agreement at the lower

Table 4. Comparison of pK_a Values for the First and Second Dissociation of *o*-Phthalic Acid in Acetonitrile/Water Mixtures at Different Temperatures with Data Reported in the Literature

ACN % (w/w)	$_s^s pK_1$							$_s^s pK_2$	
	15 °C		25 °C			35 °C		25 °C	
0	2.935[a]	2.936[b]	2.948[a]	2.950[b]	2.95[c]	2.955[a]	2.967[b]	5.395[a]	5.41[c]
10	3.201	3.324	3.201	3.316	3.15	3.193	3.310	5.847	5.77
20	3.456	3.550	3.436	3.529	----	3.411	3.518	6.375	--
30	3.690	3.710	3.655	3.681	3.60	3.620	3.672	6.865	6.86
40	3.916	3.902	3.872	3.870	3.82	3.828	3.860	7.283	7.31
50	4.145	4.193	4.096	4.162	4.08	4.054	4.144	7.673	7.75
60	4.410	4.519	4.357	4.496	----	4.316	4.476	8.095	--
70	4.761	4.471	4.703	4.472	4.77	4.657	4.518	8.604	9.06

[a] This column shows values measured in this study. [b] This column shows values taken from ref 25. [c] This column shows values in molar scale, taken from ref 13.
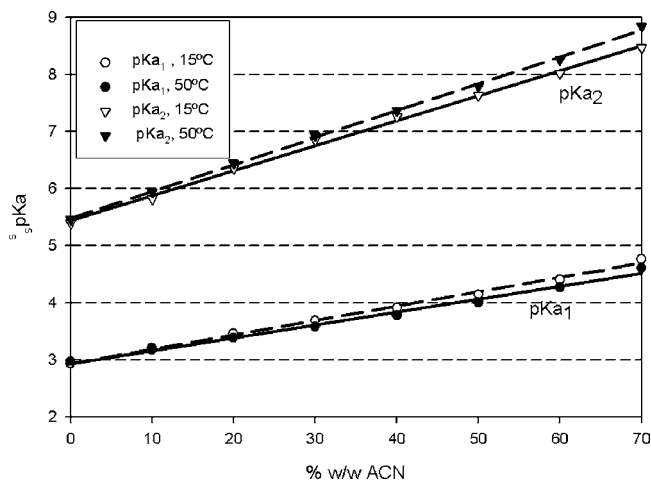
Figure 1. First (circles) and second (triangles) dissociation constants of *o*-phthalic acid in the $_s^s$pH scale at (15 and 50) °C.

acetonitrile compositions, and the differences become larger when the acetonitrile contents increase. However, it has to be stressed that the authors replaced the hydrogen electrode cell with a quinhydrone electrode for emf measurements with acetonitrile compositions above 30 % (w/w). The agreement is also good with pK_a values reported by other authors in the molar scale standard state at 25 °C.[13]

Data of pK_{a2} are reported in the literature for *o*-phthalic acid in acetonitrile/water mixtures but in the molar scale of concentrations are also compared with our results in Table 4. No other authors have reported dissociation constants of *o*-phthalic acid in acetonitrile/water mixtures in this temperature range.

Dependence of pK_a on Acetonitrile/Water Composition. To analyze the variation of the $_s^s$pK_a values with acetonitrile/water composition, both dissociation constants are plotted at two

temperatures, (15° and 50) °C, in Figure 1. It is noteworthy that $_s^s$pK_{a2} values in acetonitrile/water mixtures at high temperature are higher than $_s^s$pK_{a2} values at low temperature, whereas the variation of $_s^s$pK_{a1} is in the opposite direction. Both $_s^s$pK_a values increase linearly with the acetonitrile content in weight percentage with a larger slope in the case of the second dissociation which increases its $_s^s$pK_a value at a rate of one logarithmic unit every 20 % (w/w) change in acetonitrile content. For the first dissociation equilibrium, the increasing rate is of one logarithmic unit per increment of 40 % (w/w) in acetonitrile amount. This difference in the mentioned slopes is according to the Brönsted equation, which foresees linear relationships with a higher slope (about two times) for a monoanionic acid with respect to the corresponding neutral acid in the plots of pK_a vs the reverse of the dielectric constant of the solvent. For acetonitrile/water mixtures, the reverse of the dielectric constant increases approximately linearly with the increase of acetonitrile in the binary solvent (expressed in % w/w) in the (15 to 60) °C temperature range.[22] Therefore, a linear relationship with a positive slope should be obtained between the pK_1 and pK_2 of the *o*-phthalic acid and the solvent composition as shown in Figure 1. As expected, the slope for pK_2 is about twice the slope for pK_1. This difference in the slopes of pK_a values vs the acetonitrile−water composition leads to a constant increase in the difference between the first and second acid−base constants as the amount of organic solvent increases. The difference is of 2.5 logarithmic units in pure water, whereas it reaches 4 logarithmic units at the higher studied acetonitrile content solution. This effect increases when temperature increases. This fact recalls the question if a solution of potassium hydrogen phthalate dissolved in acetonitrile/water mixture can be considered a good buffer solution or not.

Dependence of pK_a Values on Temperature. Acidity constants in the $_s^s$pH scale are used to calculate meaningful

Table 5. Thermodynamic Quantities for the Hydrogen Ionization Reactions of *o*-Phthalic Acid in Several Acetonitrile/Water Mixtures

	first ionization reaction[a]		second ionization reaction at $\theta = 298.15$ K[b]			
	ΔH^0_1	ΔS^0_1	ΔG^0_2	ΔH^0_2	$\Delta C_p{}^0_2$	ΔS^0_2
% (w/w) ACN	kJ·mol^{-1}	J·K^{-1}·mol^{-1}	kJ·mol^{-1}	kJ·mol^{-1}	J·K^{-1}·mol^{-1}	J·K^{-1}·mol^{-1}
0	−2.0 (± 0.2)	−63	30.793 (±0.005)	−2.2 (± 0.2)	−226 (± 21)	−110
	−2.6[c]	−66[c]		−2.2[d]	−292[e]	−110[d]
10	0.9 (± 0.2)	−58	33.372 (± 0.004)	−5.8 (± 0.1)	−92 (± 16)	−132
20	3.8 (± 0.2)	−53	36.397 (± 0.004)	−5.0 (± 0.1)	−32 (± 16)	−139
30	5.8 (± 0.2)	−50	39.185 (± 0.008)	−3.6 (± 0.3)	−78 (± 31)	−144
40	6.8 (± 0.2)	−51	41.59 (± 0.01)	−4.9 (± 0.3)	−74 (± 38)	−156
50	6.8 (± 0.2)	−56	43.82 (± 0.01)	−8.3 (± 0.4)	−4 (± 50)	−175
60	7.0 (± 0.3)	−60	46.23 (± 0.01)	−12.7 (± 0.3)	86 (± 41)	−198
70	7.7 (± 0.3)	−64	49.12 (± 0.02)	−20.9 (± 0.6)	299 (± 68)	−235

[a] ΔH^0_1 calculated by linear regression (van't Hoff equation). [b] Computed from eq 7. ΔS^0_i values were calculated according to $\Delta G^0 = \Delta H^0 - T\Delta S^0$. [c] From ref 29. [d] Compiled in ref 15. [e] Compiled in ref 30.

dissociation enthalpies for both equilibria at every acetonitrile−water composition. Values of pK_{a1} and pK_{a2} were plotted as a function of the inverse of temperature, and the observation of the plots indicated that pK_{a1} variation is quite linear within this temperature range at all the acetonitrile−water compositions, but the pK_{a2} variation is not. A statistical analysis of lack of fit was conducted with both pK_{a1} and pK_{a2} data to evaluate the linearity of pK_a values with the reciprocal of temperature. At all the acetonitrile/water compositions, the analysis of variance indicated no significant curvature in the pK_{a1} against ($1/T$) plot, and thus, they follow the van't Hoff equation (ln K_a = constant − $\Delta H^0/RT$). However, the same does not apply for pK_{a2}, mainly at the extreme compositions: (0, 10, 20, and 70) % (w/w) acetonitrile. Therefore, the thermodynamic quantities for the second dissociation reaction have been estimated from Clarke and Glew's approach, which consider that $K_a(T)$ is a continuous function of temperature, so the related thermodynamic function changes, ΔG^0_T, ΔH^0_T, $\Delta C_p{}^0_T$, etc., the variations of standard Gibbs energy, enthalpy, and calorific capacity for the ionization reaction, respectively, are also well-behaved functions of T.[26−28] A reference temperature (θ) is chosen to estimate the thermodynamic function changes along with their associated standard errors. ΔH^0_T, $\Delta C_p{}^0_T$, and their successive derivatives can be expressed as a perturbation of their values at the reference temperature θ by using Taylor series expansion for each expression. The final equation is given by

$$R \ln K_a = -\frac{\Delta G^0_\theta}{\theta} - \Delta H^0_\theta\left[\frac{1}{T} - \frac{1}{\theta}\right] +$$
$$\Delta C^0_{p\theta}\left[\frac{\theta}{T} - 1 + \ln\frac{T}{\theta}\right] + \frac{\partial \Delta C^0_{p\theta}}{\partial T}... \quad (7)$$

where the last term and the following ones are truncated since they are not meaningful due to the associated errors. In this equation, ΔG^0_θ, ΔH^0_θ, and $\Delta C_p{}^0_\theta$ stand for the thermodynamic quantities of the reaction, estimated as the fitting parameters. Changes in standard entropy for both reactions were calculated from the difference between the standard free energies and the standard enthalpies. The errors associated to ΔS^0, determined by the uncertainties in ΔH^0 and ΔG^0, were estimated by error propagation rules and ranged from (± 0.7 to ± 2.0) J·mol^{-1}·K^{-1}. The results of thermodynamic quantities for both acid−base reactions are gathered in Table 5. Our estimations for these quantities in pure water are quite close to data previously published in the literature.[15,29,30] Actually, the change in enthalpy and in entropy for the second ionization reaction is coincident with those from previous studies, although the ΔS^0_1 value in pure water is somewhat smaller than that reported in the literature. However, within the experimental error, the values may be considered in good agreement. Since there is no thermodynamic ionization data in any acetonitrile/water mixture, the comparison of our measurements in these solvent mixtures is not feasible.

As shown in Table 5, the Gibbs energies (and pK_a) for both ionization reactions are dominated by the entropic contributions, which is expected for mono-, di-, and tricarboxylic acids.[29] King[31] proposed consideration of the thermodynamics of acid−base reactions in terms of external and internal contributions to both ΔH^0 and ΔS^0. The "internal" effects are those intrinsic to molecules and ions involved in the reaction, and environmental or "external" effects are those which results from the interaction of the molecules and ions with the solvent. The trends observed in the thermodynamic quantities reported in Table 5 have to be entirely attributed to the differences in solute−solvent interactions when the environment changes since
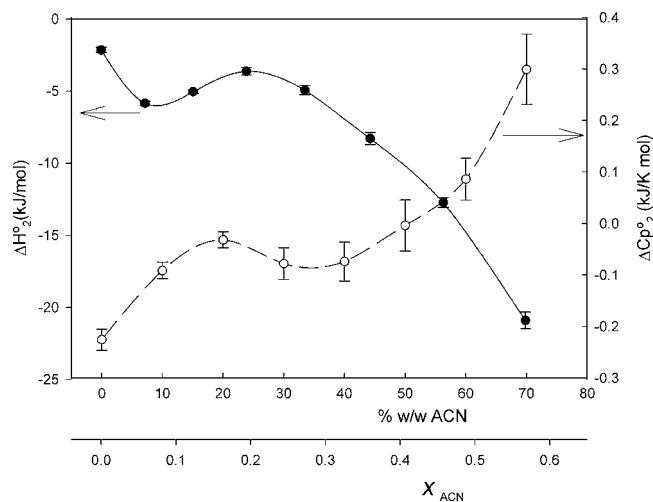

Figure 2. Dissociation enthalpy (on the left) and heat capacity (on the right) for the second dissociation equilibrium of *o*-phthalic acid as a function of solvent composition.

the internal contributions (such as the energy required to break the O−H bond, to break the intramolecular hydrogen bond, etc.) are constant.[31] Thus, the change of enthalpy for the first ionization is negligible at low acetonitrile contents and becomes endothermic when the acetonitrile mole fraction increases. In other words, for low acetonitrile contents, the temperature practically does not affect the pH of a solution buffered by this substance at values around pK_{a1}, but for higher acetonitrile contents, the increment of the temperature would effectively reduce the pH of any buffer solution prepared based on this equilibrium. The more positive ΔH^0_1 values at higher acetonitrile contents are due to different interactions of *o*-phthalic acid and its conjugated hydrogen phthalate ion with the different microenvironments.

When considering the ΔS^0_1 reported in Table 5, they are negative and present a maximum change of entropy in the region of about 30 % acetonitrile. The ions impose higher order on the surrounding solvent molecules which interfere with solvent motion. Internal entropies of ions are smaller than those of the molecules by an amount that is very nearly constant at any solvent composition.[31] Thus, the difference between the ΔS^0_1 values as the acetonitrile amount increases is due to an additional enhancement of the order of the environment of mixed solvent molecules in the extreme compositions.

The values of ΔH^0_2 and $\Delta C_p{}^0_2$ at 25 °C were computed with eq 7 and plotted as a function of acetonitrile compositions in Figure 2. The changes in enthalpy ΔH^0_2 are exothermic, are relatively small in the water-rich region, and become more negative as the relative amount of acetonitrile increases. However, it is clearly observed that this decrease is not regular, and a minimum in ΔH^0_2 occurs at about 10 % (w/w) acetonitrile, then increases up to a maximum at about 30 %, and then decreases monotonically from 30 % up to 70 % (w/w). A reversed S-shaped curve is noted for $\Delta C_p{}^0_2$ which shows a maximum around 20 % (w/w), then decreases and again increases for compositions above 40 % w/w. The rather unexpected curves portrayed in Figure 2 compelled us to make a critical evaluation of the results for this ionization reaction. Although the Clarke and Glew equation is founded on a solid theoretical basis, there is not a unique accepted method to fit Gibbs energies to some function of temperature.[32] Thus, a single linear estimation of ΔH^0_2 from the van't Hoff plot was obtained to verify the trends with solvent composition. The ΔH^0_2 values

estimated in this way follow exactly the same pattern as that shown in Figure 2.

Much attention has been paid to the physicochemical properties of acetonitrile/water mixtures. Several studies have been conducted to elucidate the liquid structure of mixtures with acetonitrile mole fraction, and it became evident that the structural properties of these mixtures are very complex.[33] Water−acetonitrile mixtures exhibit anomalous thermodynamic properties such as thermodynamics of mixing, viscosity,[34] and dielectric excess.[35] Also, several Raman,[36] X-ray,[37] NMR,[38] and fluorescence[39] spectroscopic techniques have provided evidence of a complex structure which is composition dependent. Moreau and Douheret[34] have measured transfer coefficients relative to hydrogen ion from water to water−acetonitrile mixtures at three temperatures; their results of Gibbs energies of transfer between both media show an inflection point at about $x_{ACN} = 0.03$ to 0.05, and a second inflection occurs at $x_{ACN} = 0.15$ to 0.20 depending on temperature, in close coincidence with the transitions of ΔH^0_2 trends observed in Figure 2. They suggested that it is likely due to the existence of several structural regions over the whole composition range of the water/acetonitrile mixtures. In the water-rich region ($0 < x < 0.2$) and where several extremes of excess properties are observed (excess viscosity and dielectric constant), the cavities inside the aqueous framework are progressively filled by the acetonitrile molecules. The number of neighbor water molecules is progressively reduced, due to substitution of water molecules by acetonitrile molecules. The second region covers an intermediate range, with a break at $x = 0.15$ to 0.20, as deduced also from spectroscopic measurements, and it is characterized by extreme acid−base properties. The thermodynamic quantities are thus the result of the different solvation properties of these microenvironments at each composition. Indeed, several authors postulated the microheterogeneity of acetonitrile/water mixtures at a molecular level,[34,40,41] and this term describes the situation in which molecules of each of the components are preferentially surrounded by molecules of the same kind. Marcus and Migron concluded that microheterogeneity onset at x_{ACN} higher than 0.33, whereas the acetonitrile molecule is solvated by water at lower mole fractions. More recently, Reimers and Hall[33] and Dawson and Wallen[38] proposed that microheterogeneity is a continuous phenomenon that exists over the whole composition range with structural changes occurring gradually, in contrast to the earlier models that propose sudden changes in the solvent structure which occurs at fixed compositions.

Conclusions

o-Phthalic acid ionization constants in hydrorganic mixtures from (0 to 70) % (w/w) acetonitrile and between (15 and 50) °C have been carefully measured, and the ionization thermodynamic properties (ΔG^0, ΔH^0, ΔS^0) have been calculated. The addition of organic solvent reduces the acidity of both carboxylic groups; however, the ${}^s_sK_{a2}$ decreases its value much more than ${}^s_sK_{a1}$. The effect of temperature is smaller than the effect of solvent composition but evident. Reliable ΔH^0, ΔS^0, and $\Delta C_p{}^0$ data for both acid−base equilibria have been calculated. The results confirm that these thermodynamic properties strongly depend on solvent composition. It is our opinion that reliable ΔH^0 and ΔS^0 data for acid−base equilibria in solvents other than pure water would contribute significantly to the understanding of effects involving acid−base reactions.

Literature Cited

(1) Covington, A. K.; Bates, R. G.; Durst, R. A. Definition of pH Scales, Standard Reference Values, Measurement of pH and Related Terminology. *Pure Appl. Chem.* **1985**, *57*, 531–542.

(2) Mussini, T.; Covington, A. K.; Longhi, P.; Rondinini, S. Criteria for Standarization of pH Measurements in Organic Solvents and Water+Organic Solvent Mixtures of Moderate to High Permittivities. *Pure Appl. Chem.* **1985**, *57*, 865–876.

(3) Buck, R. P.; Rondinini, S.; Covington, A. K.; Baucke, F. G. K.; Brett, C. M. A.; Camões, M. F.; Milton, M. J. T.; Mussini, T.; Naumann, R.; Pratt, K. W.; Spitzer, P.; Wilson, G. S. Measurement of pH. Definition, Standards, and Procedures. (IUPAC Recommendations 2002. *Pure Appl. Chem.* **2002**, *74*, 2169–2200.

(4) Mussini, T.; Covington, A. K.; Dal Pozzo, F.; Longhi, P.; Rondini, S.; Zou, Z. Determination of standard pH values for potassium hydrogen phthalate reference buffer solutions in 10, 20, 50, 64 and 84.2 wt. per cent methanol/water mixed solvents at temperatures from 283.15 to 313.25 K. *Electrochim. Acta* **1983**, *28*, 1593–1598.

(5) Rondinini, S.; Nese, A. Standard pH values for potassium hydrogen-phthalate reference buffer solutions in acetonitrile-water mixtures up to 70 wt % at various temperatures. *Electrochim. Acta* **1987**, *32*, 1499–1505.

(6) Barbosa, J.; Sanznebot, V. Preferential Solvation in Acetonitrile Water Mixtures - Relationship Between Solvatochromic Parameters and Standard pH Values. *J. Chem. Soc., Faraday Trans.* **1994**, *90*, 3287–3292.

(7) Rondinini, S.; Mussini, P.; Mussini, S.; Vertova, V. pH measurements in non-aqueous and mixed solvents: predicting pH(PS) of potassium hydrogen phthalate for alcohol-water mixtures (technical report. *Pure Appl. Chem.* **1998**, *70*, 1419–1422.

(8) Izutsu, K.; Yamamoto, H. Applicability of 0.05 mol kg⁻¹ potassium hydrogen phthalate as reference value pH standard in water-organic solvent mixtures. *Talanta.* **1998**, *47*, 1157–1163.

(9) Hamer, W. J.; Pinching, G. D.; Acree, S. F. First Dissociation Constant of *o*-Phthalic Acid and Related pH Values of Phthalate Buffers from 0° to 60° C. *J. Res. Natl. Bur. Stand.* **1945**, *35*, 539–564.

(10) Hamer, W.; Acree, S. Second dissociation constant of o-phthalic acid and related pH values of phthalate buffers from 0° to 60 °C. *J. Res. Natl. Bur. Stand.* **1945**, *35*, 381–416.

(11) Partanen, J. I.; Covington, A. K. Re-evaluation of the First and Second Stoichiometric Dissociation Constants of Phthalic Acid at Temperatures from (0 to 60) C in Aqueous Phthalate Buffer Solutions with or without Potassium Chloride. 1. Estimation of the Parameters for the Hückel Model Activity Coefficient Equations for Calculation of the Second Dissociation Constant. *J. Chem. Eng. Data* **2006**, *51*, 777–784.

(12) Partanen, J.; Covington, A. Re-evaluation of the First and Second Stoichiometric Dissociation Constants of Phthalic Acid at Temperatures from 0 to 60°C in Aqueous Phthalate Buffer Solutions with or without Potassium Chloride. 2. Estimation of Parameters for the Model for the First Dissociation Constant and Tests and Use of the Resulting Activity Coefficient Equations. *J. Chem. Eng. Data* **2006**, *51*, 2065–2073.

(13) Barbosa, J.; Beltran, J. L.; Sanz-Nebot, V. Ionization Constants of pH Reference Materials in Acetonitrile Water Mixtures Up to 70-Percent (W/W). *Anal. Chim. Acta* **1994**, *288*, 271–278.

(14) Barrón, D.; Buti, S.; Ruiz, M.; Barbosa, J. Preferential Solvation in the THF-Water Mixtures. Dissociation Constants of Acid Components of pH Reference Materials. *Phys. Chem. Chem. Phys.* **1999**, *1*, 295–298.

(15) Christensen, J. J.; Hansen, L. D.; Izzat, R. M. *Handbook of Proton Ionization Heats and Related Thermodynamic Quantities*; Wiley: London, 1976.

(16) Bates, R. G. *Determination of pH. Theory and Practice*; Wiley: New York, 1973.

(17) Longhi, P.; D'Andrea, F.; Mussini, P. R.; Mussini, T.; Rondinini, S. Verification of the approximate equitransference of the aqueous potassium chloride salt bridge at high concentrations. *Anal. Chem.* **1990**, *62*, 1019–1021.

(18) Izutsu, K.; Muramatsu, M.; Aoki, Y. Liquid junction potential between different solvent. A junction with different electrolytes on the two sides. *J. Electroanal. Chem.* **1992**, *338*, 125–132.

(19) Brandariz, I.; Barriada, J. L.; Taboada-Pan, C.; Sastre de Vicente, M. E. Estimating the change in liquid junction potential on glass electrodes. *Electroanalysis.* **2001**, *13*, 1110–1114.

(20) Baucke, F. G. K.; Naumann, R.; Alexander-Weber, C. Multiple-point calibration with linear regression as a proposed standardization procedure for high-precision pH measurements. *Anal. Chem.* **1993**, *65*, 3244–3251.

(21) Gagliardi, L. G.; Castells, C. B.; Ràfols, C.; Rosés, M.; Bosch, E. δ Conversion Parameter Between pH Scales (${}^s_wpH$ and ${}^spH$) in Acetonitrile/Water Mixtures at Various Compositions and Temperatures. *Anal. Chem.* **2007**, *79*, 3180–3187.

(22) Gagliardi, L.; Castells, C.; Ràfols, C.; Rosés, M.; Bosch, E. Static Dielectric Constants of Acetonitrile/Water Mixtures at Different Temperatures and Debye-Hückel A and a₀B Parameters for Activity Coefficients". *J. Chem. Eng. Data* **2007**, *52*, 1103–1107.

(23) Inczedy, J.; Lengyel, T.; Ure, A. (ed.) *IUPAC. Compendium on Analytical Nomenclature. Definitive Rules 1997*; Blackwell Science: Oxford, 1998.

(24) Bates, R.; Guggenheim, E. Report on the standarization of pH and related terminology. *Pure Appl. Chem.* **1960**, *1*, 163–168.

(25) Rondinini, S.; Nesse, A. Standard pH Values for Potassium Hydrogen Phtalate Reference Buffer Solutions in Acetonitrile-Water Mixtures up to 70 wt % at Various Temperatures. *Electrochim. Acta* **1987**, *32*, 1499–1505.

(26) Clarke, E. C.; W. Glew, D. N. Evaluation of Thermodynamic Functions from Equilibrium Constants. *Trans. Faraday Soc.* **1966**, *62*, 539–547.

(27) Butikofer, H. P.; Covington, A. K.; Evans, D. A. New data analysis method for the evaluation of ionization constants and other thermodynamic functions from the temperature dependence of the electromotive force of cells. *Electrochim. Acta* **1979**, *24*, 1071–1079.

(28) Covington, A. K.; Zou, Z. Y. Application of multilinear regression analysis to the evaluation of the standard emf of the hydrogen-silver/silver chloride cell in methanol+water mixtures over wide ranges of temperature and composition. *Electrochim. Acta* **1983**, *28*, 1587–1591.

(29) Christensen, J.; Izzat, R.; Hansen, L. Thermodynamics of Proton Ionization in Dilute Aqueous Solution. VII. DH and DS Values for Proton Ionization from Carboxylic Acids at 25°C. *J. Am. Chem. Soc.* **1967**, *89*, 213–222.

(30) Goldberg, R.; Kishore, N.; Lennen, R. Thermodynamic Quantities for the Ionization Reactions of Buffers. *J. Phys. Chem. Ref. Data.* **2002**, *31*, 231–370.

(31) King, E. *Acid-Base Equilibria*; Pergamon Press: New York, 1965.

(32) Castells, R.; Arancibia, E.; Nardillo, A.; Castells, C. Thermodynamics of hydrocarbon solutions using g.l.c. n-Hexane, n-heptane, benzene and toluene as solutes each at infinite dilution in n-hexadecane, n-octadecane and n-eicosane. *J. Chem. Thermodyn.* **1990**, *22*, 969–977.

(33) Reimers, J.; Hall, L. The Solvation of Acetonitrile. *J. Am. Chem. Soc.* **1999**, *121*, 3730–3744.

(34) Moreau, C.; Douhéret, G. Solvation Ionique dans les Mélanges Eau-Acetonitrile. Structure de Ceux-Ci. *J. Chim. Phys.* **1974**, *71*, 1313–1321.

(35) Moreau, C.; Douhéret, G. Thermodynamic and Physical Behaviour of Acetonitrile + Water Mixtures. Dielectric Properties. *J. Chem. Thermodyn.* **1976**, *8*, 403–410.

(36) Rowlen, K. L.; Harris, J. M. Raman Spectroscopy Study of Solvation Structure in Acetonitrile/Water Mixtures. *Anal. Chem.* **1991**, *63*, 964–969.

(37) Takamuku, T.; Tabata, M.; Yamaguchi, A.; Nishimoto, J.; Kumamoto, M.; Wakita, H.; Yamaguchi, T. Liquid Structure of Acetonitrile-water mixtures by X-ray diffraction and infrared spectroscopy. *J. Phys. Chem. B* **1998**, *102*, 8880–8888.

(38) Dawson, E.; Wallen, S. Probing transport and microheterogeneous solvent structure in acetonitrile-water mixtures and reversed-phase chromatographic media by NMR quadrupole relaxation. *J. Am. Chem. Soc.* **2002**, *124*, 14210–14220.

(39) Kovacs, H.; Laaksonen, A. Molecular dynamics simulation and NMR study of water-acetonitrile mixtures. *J. Am. Chem. Soc.* **1991**, *113*, 5596–5605.

(40) Marcus, Y.; Migron, Y. Polarity, Hydrogen Bonding, and Structure of Mixtures of Water and Cyanomethane. *J. Phys. Chem.* **1991**, *95*, 400–406.

(41) Easteal, A. A Luminescent Probe Study of Water/Acetonitrile Mixtures. *Aust. J. Chem.* **1979**, *32*, 271–275.