

The Influence of Solvent in Binary Acetonitrile – Water Solvent Systems on Dissociation Constants of Protonated Pyridine and Its *N*-Oxide

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Using a 2,6-dinitrophenol – tetra-*n*-butylammonium 2,6-dinitrophenolate standardizing system, the application of the previously proposed method for pK_a determination of potentiometric standards in binary solvent systems consisting of an organic polar solvent (acetonitrile in this case) and water was checked. The reliability of the obtained pK_a values of 2,6-dinitrophenol was checked in a system of protonated pyridine in acetonitrile – water mixtures over the range of 0 through 1 mole fraction of acetonitrile, for which literature data were available. The method checked in this way was subsequently used to determine pK_a of protonated pyridine *N*-oxide in this binary solvent system. pK_a values served for discussion of the variations of pK_a 's of cationic acids conjugated with pyridine and its *N*-oxide and of the influence of composition of the binary solvent.

Key words: binary solvent systems acetonitrile – water, cationic acid dissociation, pyridine, pyridine *N*-oxide

Mixtures of solvents are interesting, because two solvents may produce systems with entirely different physical (electric permittivity, density, and viscosity) and chemical (acid-base properties, electron donor and acceptor properties) characteristics as compared to those of single constituent [1]. Variations of solvent properties may be accompanied by variations of the properties of dissolved electrolytes, including the strength of acids and bases. Of particular importance is the proton-donating and proton-accepting properties of the solvent, as well as its polarity. By mixing solvents of different polarities electric permittivity of the medium can be varied and, consequently, the strength of dissolved acids and bases [2].

Another reason for the variations of the mixed solvent properties are solvent-solvent interactions. These are weaker than the ion-solvent ones, but affect the processes occurring in mixed solvents [3]. Very important are structural variations of solvent mixtures [4] responsible for structural changes of individual constituents of the mixtures. In mixtures of aprotic solvents with water the structure of water has been found to be destroyed by such polar aprotic solvents as acetonitrile [5], acetone [6], sulfolane [5], propylene carbonate [7] and dimethyl sulfoxide [5].

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As consequences of the deviations from the Born equation, as well as the structural changes, are probably the reported [4,8] non-linear pK_a variations of acids and phenols with composition of the solvent mixtures, involving the probability of appearance of extremum of pK_a 's. A similar case is with cationic acids. Both with mixtures of aprotic solvent – water and amphiprotic solvent – water types, the pK_a 's of cationic acids pass through a minimum with varying mixed solvent composition [9]. This is due to a progressive destruction of the water structure with increasing organic solvent concentration [10].

A model structure of a mixed solvent has been proposed for the acetonitrile – water systems [11–13]. According to this model, three regions can be distinguished of acetonitrile mole fractions, namely 0 – 0.2, 0.2 – 0.8 and 0.8 – 1. In the first region, an increase in acetonitrile content results in breaking of H-bonded chains of the primary water structures to form lone pairs of water molecules and water molecules associated with polar acetonitrile molecules. In the second region (0.2 – 0.8), big aggregates are gradually broken up into smaller particles dominated by dihydrates. In the third region, with a large excess of acetonitrile, the structure of water is completely destroyed.

The purpose of this contribution was to determine the acid dissociation constants:



in systems of protonated pyridine and protonated pyridine *N*-oxide in the binary acetonitrile – water systems with acetonitrile mole fractions x ranging between 0 and 1 at 0.1 increments. The pK_a 's should provide a basis for verification of the already proposed [1] procedure of pK_a determination in the binary solvents mixtures in the case of acetonitrile – water systems on one hand, and the aforementioned model of the acetonitrile – water system, on the other hand. Moreover, they should enable to compare the influence of water on acid-base properties of both heterocyclic bases carrying the oxygen and nitrogen centres.

EXPERIMENTAL

The e.m.f. measurements of the cell: indicator glass electrode | system studied | | modified calomel electrode were run using an OP-7183 (Radelkis) indicator glass electrode and an OP-08303 (Radelkis) reference calomel electrode. A modified calomel electrode, placed in a shortened salt bridge filled with a 0.01 M tetra-*n*-butylammonium perchlorate solution in a binary solvent mixture with $x_{AN} = 0.5$ was used. The modification consisted in replacing the potassium chloride solution by a 0.1 M tetra-*n*-butylammonium chloride solution in the mixed solvent of composition identical to that in the salt bridge. The e.m.f. measurements of the perchlorate of base studied (pyridine *N*-oxide or pyridine) – base studied (pyridine *N*-oxide or pyridine) systems were run at a constant ionic strength. The solution containing perchlorate of base studied ($BHClO_4$) at a concentration of about 0.001 M was titrated with the solution containing the base (B) at a concentration of about 0.01 M and $BHClO_4$ at the same concentration as that of the titrand (to keep the formal ionic strength constant for all titration points). The glass electrode used for potentiometric measurements was calibrated before each series of measurements against a 2,6-dinitrophenol – tetra-*n*-butylammonium 2,6-dinitrophenolate buffer solution at a constant ionic strength. 0.001 M tetra-*n*-butylammonium 2,6-dinitrophenolate solution was titrated with a solution containing 2,6-dinitrophenol and tetra-*n*-butylammonium 2,6-dinitrophenolate at a concentration of 0.01 M and 0.001 M,

respectively, in order to keep the formal ionic strength constant. The previously purified solvents were mixed at appropriate mole fractions. Acetonitrile (AN) was purified by the modified Coetzee method [14]. At first the solvent was dried with CaH_2 (10 g/dm^3) for 48 h. After decantation acetonitrile was distilled over P_2O_5 (3 g/dm^3). The distillate was dried again with CaH_2 and distilled after 48 h. Water (W) was purified by triple distillation. The purified solvents had a specific conductivity of $4\text{--}10 \times 10^{-8}$ and $1\text{--}5 \times 10^{-7} \text{ S cm}^{-1}$, respectively. Simple 1:1 salts of the N-oxides with perchloric acid were obtained by mixing together equivalent quantities of a 72% aqueous perchloric acid with base in methanol. The mixture was vacuum concentrated. The residue was filtered off, washed twice with chloroform and dried in vacuum over P_2O_5 . 2,6-Dinitrophenol was purified by triple crystallization from methanol. Tetra-n-butylammonium 2,6-dinitrophenolate was obtained by mixing together equimolar quantities of the purified 2,6-dinitrophenol with 25% tetra-n-butylammonium hydroxide in methanol. The salt was crystallized twice from ethyl acetate. Tetra-n-butylammonium perchlorate was obtained by mixing together equimolar quantities of 72% aqueous HClO_4 solution with 25% tetra-n-butylammonium hydroxide in methanol. Both salts were crystallized twice from ethanol. Tetra-n-butylammonium chloride was purified by triple crystallization from a 1:1 mixture acetonitrile and ethyl acetate. Potentials were measured with the precision of $\pm 0.1 \text{ mV}$ by using a multifunctional CX-731 (ELMETRON) apparatus. All measurements were run at $T = 298.1 \pm 0.1 \text{ K}$.

RESULTS AND DISCUSSION

As mentioned above, the linearity of the response of the glass electrode vs. the modified calomel electrode was checked by the system: 2,6-dinitrophenol – tetra-n-butylammonium 2,6-dinitrophenolate. The relationships $E = f(\log c_{\text{HA}}/c_{\text{A}^-})$, where HA denotes 2,6-dinitrophenol and A^- denotes the conjugated 2,6-dinitrophenolate anion were linear in the wide range of the concentrations ratio and the slopes of the glass electrode characteristics were close to Nernst value 59.14 mV . The first major problem of this study was that there was no literature value for the pK_a of 2,6-dinitrophenol, used as a reference compound in the standardizing system with tetra-n-butylammonium 2,6-dinitrophenolate in the solvent mixtures studied. There are only literature values in solvents used for the preparation of the binary mixtures. They equal 16.45 and 3.73 for acetonitrile [15] and water [16], respectively. Thus, the pK_a values in the solvents mixtures studied have been determined by the procedure already proposed by us [1]. This means that pK_a values were determined from the difference in the e.m.f. of solutions containing equimolar proportions of both buffer components in the solvent mixture and in one of mixture components, based on the following equations:

$$\text{pK}_a^x = \text{pK}_a^{\text{AN}} - \frac{(E_{1/2}^x - E_{1/2}^w) \cdot \Delta\text{pK}_a}{\Delta E_{1/2}} \quad (2)$$

where:

$$\Delta\text{pK}_a = \text{pK}_a^{\text{AN}} - \text{pK}_a^w; \quad \Delta E_{1/2} = E_{1/2}^{\text{AN}} - E_{1/2}^w \quad (3,4)$$

pK_a^x is the pK_a value of 2,6-dinitrophenol in a mixture of acetonitrile with water (concentration of acetonitrile in the mixture is shown by the mole fraction x); pK_a^w stands for the pK_a value of 2,6-dinitrophenol in water and pK_a^{AN} for the pK_a value of 2,6-dinitrophenol in acetonitrile; $E_{1/2}^x$ denotes the e.m.f. in solution containing

equimolar quantities of 2,6-dinitrophenol and conjugate anion in a mixture of acetonitrile (of concentration x expressed in mole fraction) with water; $E_{1/2}^w$ stands for the e.m.f. in solution of equimolar quantities of 2,6-dinitrophenol and conjugate anion in water and $E_{1/2}^{AN}$ for the e.m.f. in solution of equimolar quantities of 2,6-dinitrophenol and conjugate anion in acetonitrile. The pK_a^x values of 2,6-dinitrophenol determined in this way enabled to calibrate the measuring system in the solvent mixtures studied.

The pK_a^x values of 2,6-dinitrophenol in acetonitrile – water mixtures with acetonitrile mole fractions x are collected in Table 1. A relationship between pK_a^x and the mole fraction of acetonitrile is shown in Fig. 1. The relationship is non-linear, the pK_a^x for 2,6-dinitrophenol is attaining a minimum in the x range of 0.4–0.5. It should be noted that the pK_a^x values for 2,6-dinitrophenol are lower than those in water by almost 7 (exactly 6.68) pK_a units. It should also be emphasised that by extrapolation of the branches of the curve corresponding to the excess of water ($x < 0.3$) and the excess of acetonitrile ($x > 0.7$) almost accurate literature pK_a 's for 2,6-dinitrophenol in water (3.73) and acetonitrile (16.45), respectively, could be obtained. This can provide a confirmation for the reliability of the pK_a^x values for 2,6-dinitrophenol in the acetonitrile – water systems studied. Parameters s (slope of the response of the glass electrode) and E^o (standard e.m.f.), obtained from potentiometric titrations in standardizing systems together with the results of the potentiometric titrations carried out in the systems B_1H^+/B served as a basis for the determination of the acidity constant values in mixed media studied. To calculate the constants from potentiometric results the program STOICHIO [17–19] was used. This program can handle any model of chemical equilibria and determines the equilibrium constant values as parameters of the function to be minimised using Marquardt's method. This method enables to take into account not only the errors in the e.m.f., but also those in titration volume, stock-solution preparation, electrode calibration parameters, reagent impurities, as well as the equilibrium constants determined from other measurements.

Table 1. pK_a values of 2,6-dinitrophenol in the acetonitrile – water systems at 298.1 K.

x	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
pK_a^x	3.73 ^a	1.96	0.01	-1.42	-2.74	-2.95	-1.27	1.55	5.65	9.20	16.45 ^b

^a From [15]; ^b From [16].

In the first step, the pK_a values were then determined for protonated pyridine in the solvent systems using the aforementioned computational procedure. These systems provided a kind of test system, because pK_a^x 's for this cationic acid are known for some mole fractions of acetonitrile [20]. The pK_a^x 's for protonated pyridine, calculated by the general method of Kostrowicki and Liwo based on pK_a 's of 2,6-dinitrophenol, determined by the procedure described above are listed in Table 2. Closer inspection of these results shows that the relation is, as expected, non-linear, the pK_a^x 's of protonated pyridine is attaining a minimum at x in the range 0.4–0.5. It

should be noted that the minimum values are lower than those of pK_a of protonated pyridine in water by approximately 0.6 (0.59) pK_a unit. Similar relationships have been reported for the dimethyl sulfoxide and *N*-methylpyrrolidone – water systems [9]. It can be concluded, therefore, that solute-solvent interactions rather than the electric permittivity play a primary role in the isoelectric dissociation process of cationic acid of BH^+ type. By measurement of Gibbs transfer energies it has been shown [21,20] that these results are attributable to selective solvation of the individual species involved in the equilibrium. Thus, in acetonitrile – water binary mixtures containing cationic acids selective solvation by one component is also preferred. Especially the proton, owing to its intense electrical field, is preferentially solvated by the more polar molecules, in this case water molecules. For the sake of comparison, in Table 2 are also shown literature pK_a^x values for protonated pyridine [20] in some binary acetonitrile – water systems. As seen, the values determined in this work are in good agreement with the previous ones. Some disparity occurs at $x = 0.8$. Nonetheless, even these values can be considered as consistent ones when taking into account their standard deviation. Thus these results confirmed the usefulness of such investigations aimed at determination of pK_a 's of cationic acids in binary solvent systems including acetonitrile – water ones.

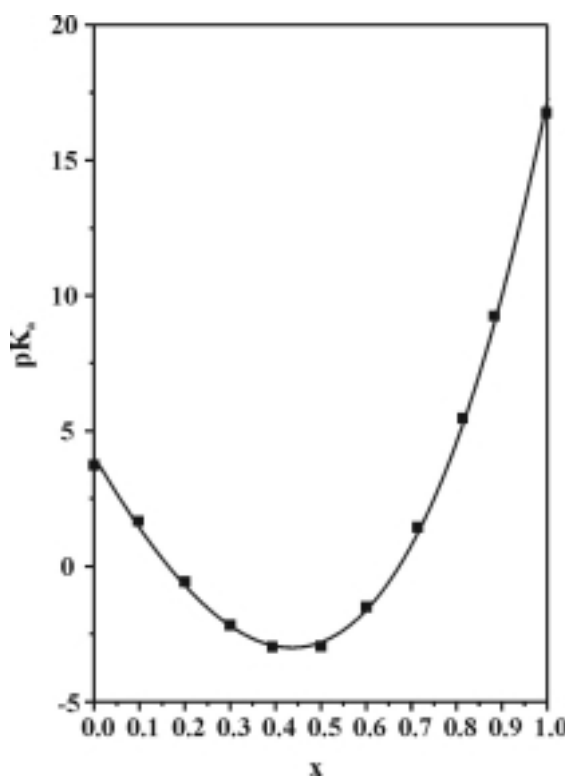


Figure 1. The influence of the acetonitrile – water system composition, $\{x_{AN} + (1-x)_W\}$, on pK_a of 2,6-dinitrophenol, at 298.1 K.

Table 2. The determined pK_a values of protonated pyridine (standard deviations in parentheses) in the acetonitrile – water systems and the calculated standard molar Gibbs free energies (kJ mol^{-1}) for the transfer from aqueous solution to the binary solvent systems, ΔG_m° at 298.1 K. For comparison, literature pK_a values are included for some x values.

x	This work		Literature data	
	pK_a^x	ΔG_m°	pK_a^x	ΔG_m°
0			5.22 ^a	
0.1	4.96(0.05)	–1.5		
0.2	4.78(0.06)	–2.5	4.87 ^b	–2.0 ^b
0.3	4.70(0.09)	–3.0		
0.4	4.63(0.10)	–3.4	4.53 ^b	–3.9 ^b
0.5	4.63(0.12)	–3.4		
0.6	4.64(0.18)	–3.3	4.61 ^b	–3.5 ^b
0.7	4.76(0.21)	–2.6		
0.8	5.57(0.26)	2.0	5.07 ^b	–0.8 ^b
0.9	6.93(0.26)	9.8		
1			12.47 ^c	

^a From [23]; ^b From [20]; ^c From [24].

Assuming, the method to be reliable, it was subsequently employed for the determination of pK_a 's of protonated pyridine *N*-oxide in the acetonitrile – water systems. The determined pK_a^x values are shown in Table 3, and a relationship between pK_a^x of the protonated pyridine *N*-oxide and x is shown in Fig. 2. Analysis of the determined constants shows that their variability is similar to that of the protonated pyridine, the lowest pK_a 's fall in the x range of 0.4–0.5, thus being lower than those for water by 1.3 (1.29) pK_a units. Consequently, these variations are almost twice as high as those of the protonated pyridine. Moreover, with the protonated pyridine *N*-oxide, pK_a^x attains a value characteristic of aqueous solutions (0.79) for the mole fraction of acetonitrile of about 0.7, whilst for the protonated pyridine that value was approximately equal to 0.8.

Table 3. pK_a values of the protonated pyridine *N*-oxide (standard deviations in parentheses) in the acetonitrile – water systems and the calculated standard molar Gibbs free energies (kJ mol^{-1}) for the transfer from aqueous solution to the binary solvent systems, ΔG_m° at 298.1 K.

x	pK_a^x	ΔG_m°
0	0.79 ^a	
0.1	0.18(0.07)	–3.5
0.2	–0.30(0.06)	–6.2
0.3	–0.35(0.08)	–6.5
0.4	–0.50(0.06)	–7.4
0.5	–0.40(0.08)	–6.8
0.6	–0.05(0.07)	–4.8
0.7	0.51(0.12)	–1.6
0.8	3.06(0.12)	13.0
0.9	4.93(0.10)	23.6
1	10.04 ^b	

^a From [23]; ^b From [24].

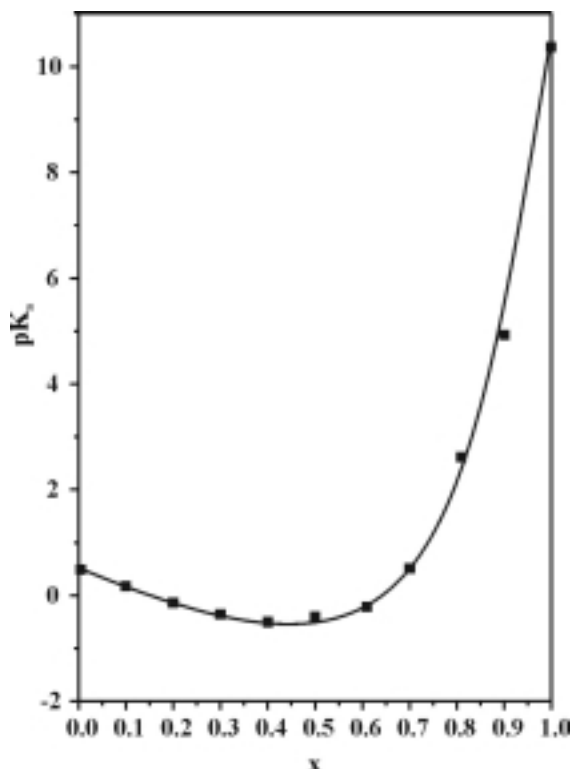


Figure 2. The influence of composition of the acetonitrile – water system, $\{x_{\text{AN}} + (1-x)_{\text{w}}\}$, on pK_{a} of the protonated pyridine *N*-oxide, at 298.1 K.

The Gibbs free energy changes for the transfer from aqueous solutions to the mixed solvents, which accompany the pK_{a} variations, were calculated by:

$$\Delta G_{\text{m}}^{\circ} = -RT \ln 10 \Delta \text{pK}_{\text{a}} = 5\,707 (\text{pK}_{\text{a}}^{\text{x}} - \text{pK}_{\text{a}}^{\text{w}}) [\text{J} \cdot \text{mol}^{-1}] \quad (5)$$

both for the protonated pyridine and protonated pyridine *N*-oxide. They are collected in Tables 2 and 3. Minimum $\Delta G_{\text{m}}^{\circ}$ values, similar to the minimum pK_{a} values in these systems, fall in the mole fraction range of acetonitrile of 0.4–0.5. Just for these x values the strongest solvent-solvent interactions have been postulated. Further, the $\Delta G_{\text{m}}^{\circ}$ values for the protonated pyridine *N*-oxide are almost twice lower than those for the protonated pyridine. This indicates that stabilization of the proton in the binary acetonitrile – water systems is energetically preferred with a cationic acid conjugated with pyridine *N*-oxide over the cationic acid obtained by protonation of the parent pyridine.

CONCLUSIONS

- i) The previously proposed method [1] of pK_{a} determination of cationic acids in binary organic solvent systems can be also used in binary mixtures of organic polar solvents (acetonitrile in this case) and water.

- ii) A model structure of a mixed solvent proposed [11–13] for the acetonitrile – water systems can be also applied in the case of cationic acids conjugated with organic oxygen bases.
- iii) The stabilization of the proton in the binary acetonitrile – water systems in the case of the cationic acid conjugated with pyridine *N*-oxide is energetically preferred with respect to the cationic acid conjugated with the parent pyridine.
- iv) Both the non-linear variation of the pK_a values of 2,6-dinitrophenol as a function of composition of the acetonitrile – water mixtures and the local minimum (in the x range 0.4–0.5) of pK_a can be observed.

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