Monatshefte für Chemie 124, 127–133 (1993)

Monatshefte für Chemie
Chemical Monthly

Medium Effects on the Acid Dissociation Constants of Some Diimine Heterocyclic Bases

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Abstract. The acid dissociation constants of the protonated form of diimine heterocyclic compounds (imidazole, 2-methylimidazole, 2,2′-bipyridyl, and 1,10-phenanthroline) were determined *pH*-meterically in aqueous media containing different amounts of organic solvents, viz. amphiprotic (methanol, ethanol), dipolar aportic (*DMSO*), and low basic aprotic (acetonitrile) at 25 ± 0.1 °C. It was observed that by increasing the amount of alcohol or *DMSO* in the aqueous medium the pK_a, values of the investigated compounds decreased. On the other hand, the pK_a values increased as the amount of acetonitrile in the medium was increased. These results are discussed in terms of various solvent characteristics. It is concluded that solvent effects, viz. differences in stabilization of the free base by dispersion forces and of the proton by its interaction with solvent molecules in amphiprotic or dipolar aprotic solvent-aqueous media relative to that in pure aqueous one, as well as the basicity effect of acetonitrile play a vital role in the ionisation equilibria of the investigated compounds.

Keywords. Medium effects; Acid dissociation constants; Dissociation of diimine heterocyclic bases; Solvent effects; Acid-base equilibrium.

Mediumeffekte auf die Säuredissoziationskonstanten einiger heterocyclischer Diimin-Basen

Zusammenfassung. Die Säuredissoziationskonstanten der protonierten Formen der heterocyclischen Dimin-Basen Imidazol, 2-Methylimidazol, 2,2′-Bipyridyl und 1,10-Phenanthrolin wurden *pH*-metrisch in wäßrigem Medium mit einem Anteil an organischen Lösungsmitteln bei 25 ± 0.1 °C bestimmt. Dabei wurden als amphiprotische Zusätze Methanol und Ethanol, als dipolar aprotisches organisches Lösungsmittel *DMSO* und als aprotisches niederer Basizität Acetonitril ausgewählt. Es wurde beobachtet, daß bei ansteigenden Konzentrationen an Alkohol oder *DMSO* die pK_a-Werte der untersuchten Verbindungen kleiner werden. Andererseits bewirkt Acetonitril ein Ansteigen der pK_a-Werte. Die Ergebnisse werden mittels verschiedener Lösungsmittelparameter diskutiert. Lösungsmitteleffekte wie Stabilisierung der freien Base mittels Dispersionskräften, Protonwechselwirkungen in den verschiedenen Lösungsmittelgemischen und Basizitätseffekte des Acetonitril spielen dabei eine entscheidende Rolle.

Introduction

Though heterocyclic diimines (imidazole, 2-methylimidazole, 2,2′-bipyridyl, and 1,10-phenanthroline) represent a very interesting class of compounds from the biological and analytical point of view, not much attention has been paid to the medium effects on the acid dissociation constants of such compounds. Vasil'ev, Grechina and Ziatseva [1] studied the acid-base properties of imidazole in water-*DMSO* mixtures. The thermodynamic properties of 2,2′-dipyridinium and 1,10-phenanthrolinium ions were investigated pH-metrically or spectrophotometrically in aqueous media containing different amounts of organic solvents, viz. *tert*-butanol, glycerol [2], methanol [3], ethanol [4], iso-propanol [5], ethanediol [6], 2-methoxyethanol [7], 1,2-dimethoxyethane [7], and formamide, dimethylformamide [8]. In the present article a systematic pH-metrical study for the determination of the acid dissociation constants of the protonated forms of some diimine heterocyclic bases in aqueous solutions containing varying proportions of amphiprotic solvents (methanol, ethanol), dipolar aprotic solvents (dimethylsulfoxide) and low-basic aprotic solvents (acetonitrile) has been carried out. The obtained pK_a values are discussed in terms of solvent characteristics.

Experimental

The heterocyclic diimines used were Merck or BDH A.R. products. The organic solvents (methanol, ethanol, *DMSO*, and acetonitrile) were of high purity (A.R. or spectral grade products).

Stock solutions of diimine heterocyclic compounds were prepared by dissolving an accurate amounts of each in the proper organic solvent. A 0.2 mol dm^{-3} NaOH solution was prepared by

Table 1. Mean pK_a values for imidazole and 2-methylimidazole in different organic solvent-water mixtures at 25 °C ± 0.1 °C

Organic solvent	% ω/ω of organic solvent	Mole fraction of organic solvent (X)	Dielectric constant of the medium at 25 °C	$1/D \times 10^2$	pK_a	
					Imidazole	2-Methylimidazole
*Me*OH	zero	zero	78.40	1.276	6.75±0.02[a]	7.77±0.02[b]
	20	0.123	72.77	1.374	6.73±0.01	7.74±0.01
	40	0.270	66.03	1.518	6.47±0.01	7.57±0.01
	60	0.457	57.47	1.739	6.17±0.01	7.33±0.02
*Et*OH	zero	zero	78.40	1.276	6.75±0.02	7.77±0.02
	20	0.088	71.50	1.398	6.62±0.01	7.74±0.01
	40	0.207	67.20	1.488	6.45±0.02	7.48±0.01
	60	0.369	58.44	1.711	6.26±0.01	7.26±0.02
DMSO	zero	zero	78.40	1.276	6.75±0.02	7.77±0.02
	20	0.054	76.68	1.304	6.66±0.01	7.61±0.02
	40	0.133	74.17	1.348	6.35±0.02	7.25±0.01
	60	0.257	70.23	1.424	5.83±0.02	6.87±0.02
Acetonitrile	zero	zero	78.40	1.276	6.75±0.02	7.77±0.02
	20	0.099	74.20	1.348	6.68±0.01	7.85±0.01
	40	0.225	68.86	1.452	6.83±0.01	7.92±0.01
	60	0.397	61.57	1.624	7.04±0.03	8.15±0.02

[a] The reported pK_a value, Ref. [21] is 7.13, Ref. [23] 6.95

[b] The reported pK_a value, Ref. [22] is 8.00, Ref. [23] 7.86

dissolving the analar NaOH pellets in CO_2 free bidistilled water and the solution was standardized with a standard 0.2 mol dm^{-3} potassium hydrogen phthalate. A 1.0 mol dm^{-3} stock solution of $NaClO_4$ was used as supporting electrolyte. Generally, dilute solutions were prepared by appropriate dilution of the stock.

The pK_a values of the heterocyclic diimines in different organic solvent-water mixtures were determined by adopting the Irving and Rossotti pH-titration technique [9, 10]. pH-titrations were carried out with a standard carbonate-free NaOH on solutions (50 ml) containing:

a) $HClO_4$ ($4.9-5.5 \times 10^{-3}$ mol dm^{-3}) + $NaClO_4$ (0.1 mol dm^{-3});
b) Solution (a) in presence of 5×10^{-3} mol dm^{-3} of heterocyclic diimines and containing different proportions (ω/ω) of the organic solvent.

The pH-meter readings (taken at 25 °C using a Schott Gerate model CG 822 pH-meter) have been corrected in accordance with the method described by Douheret [11, 12]. This was carried out to account for the difference in acidity, basicity, dielectric constant, and ion activities in partially aqueous solutions relative to the pure one.

The pK_a values were calculated using three different methods. These methods were computer analysis, the graphical method (average value method) and the linear plot method. The mean pK_a values of these methods are collected in Tables 1 and 2.

Owing to the sparingly soluble character of 2,2′-bipyridyl and 1,10-phenanthroline it was not possible to determine the acid dissociation constants of these compounds in pure aqueous media.

Table 2. Mean pK_a values for 2,2′-bipyridyl and 1,10-phenanthroline in different organic solvent-water mixtures at 25 ± 0.1 °C

Organic solvent	% ω/ω of organic solvent	Mole fraction of organic solvent (X)	Dielectric constant of the medium at 25 °C	$1/D \times 10^2$	pK_a	
					2,2′-Dipyridyl	1,10-Phenanthroline
*Me*OH	30	0.194	69.51	1.441	4.17 ± 0.01	4.24 ± 0.01
	40	0.270	66.03	1.519	3.97 ± 0.02	4.11 ± 0.02
	50	0.359	61.96	1.618	3.77 ± 0.02	3.93 ± 0.03
	60	0.457	57.47	1.739	3.52 ± 0.10	3.76 ± 0.02
*Et*OH	30	0.140	70.83	1.412	3.94 ± 0.02	4.31 ± 0.01
	40	0.207	67.20	1.488	3.75 ± 0.01	4.07 ± 0.01
	50	0.280	63.25	1.579	3.74 ± 0.01	3.83 ± 0.01
	60	0.369	58.44	1.711	3.59 ± 0.02	3.66 ± 0.02
DMSO	30	0.090	75.54	1.324	3.81 ± 0.01	4.16 ± 0.02
	40	0.133	74.17	1.348	3.65 ± 0.01	4.01 ± 0.01
	50	0.187	72.45	1.380	3.61 ± 0.01	3.73 ± 0.01
	60	0.257	70.23	1.424	3.23 + 0.01	3.57 + 0.01
Acetonitrile	30	0.160	71.62	1.396	4.18 ± 0.01	4.50 ± 0.01
	40	0.225	68.86	1.452	4.29 ± 0.01	4.56 ± 0.02
	50	0.305	65.47	1.527	4.60 ± 0.01	4.72 ± 0.02
	60	0.397	61.57	1.624	4.60 ± 0.02	4.88 ± 0.02

Results and Discussion

The mean pK_a values of the protonated forms of the diimine heterocyclic bases in different aquo-organic solvent mixtures are listed in Tables 1 and 2. These results reveal that the pK_a values of all investigated compounds are largely dependent on both the proportion and the nature of the organic co-solvent used. Generally, the acid dissociation constant of the protonated form of each of the investigated compounds increases as the amount of the amphiprotic solvent (methanol or ethanol) or the dipolar aprotic *DMSO* in the aqueous media is increased. On the other hand the acid dissociation constant of each compound decreases as the amount of the low basic aprotic solvent acetonitrile in the medium is increased.

Effect of Amphiprotic and Dipolar Aprotic Solvents

The acid-base equilibrium of the ionisation step of the protonated form of the investigated compounds can be represented by the following equation:

$$\mathrm{H}B^+ \rightleftharpoons \mathrm{H}^+ + B.$$

According to Coetzee and Ritchie [13] the acid dissociation constant in aqueous medium (K_a) is related to that in partially aqueous medium (K'_a) by the relation:

$$K_a = K'_a \cdot \gamma_{\mathrm{H}^+} \cdot \gamma_B / \gamma_{\mathrm{H}B^+},$$

where γ is the activity coefficient of the subscripted species in a partially aqueous medium relative to that in a pure one. It is known that the electrostatic effect resulting from the change in dielectric constant of the medium operates on the activity coefficient of any charged species [13]. The magnitude of this effect is inversely proportional to the radius of the ionic species considered [14]. Consequentely the magnitude of this effect on the proton exceeds that on the acid form $\mathrm{H}B^+$. Thus the acid dissociation constant value of the protonated form of these compounds is expected to decrease with increase in the proportions of the organic solvent in the medium. This is not the case as it is evident from the results reported in Table 1 and 2. Accordingly, factors other than the electrostatic one played the major role in determining the effect of the amphiprotic or dipolar aprotic solvent on the acid dissociation process of these compounds. This suggestion is further substantiated by the obtained nonlinear relationship on plotting pK_a against $1/D$ of the medium [15, 16] (Fig. 1).

Generally, the amphiprotic solvents methanol or ethanol are characterized by relatively low basicity compared to pure water. Thus one can deduce that changing the medium basicity by increasing additions of methanol or ethanol to the aqueous medium has little influence on the acid dissociation process of the heterocyclic diimine compounds.

Furthermore, since water molecules are characterized by a greater tendency to donate hydrogen bonds as compared with other solvent molecules [17], the free bases of the studied compounds are expected to be less stabilized by hydrogen bonding interaction with solvent molecules as the amount of the organic co-solvent in the medium is increased (i.e. γ_B increases). Thus, the acid dissociation constant of the protonated form of the studied compounds should decrease with increase in the amount of co-organic solvent (alcohol or *DMSO*) in the medium. However, this is

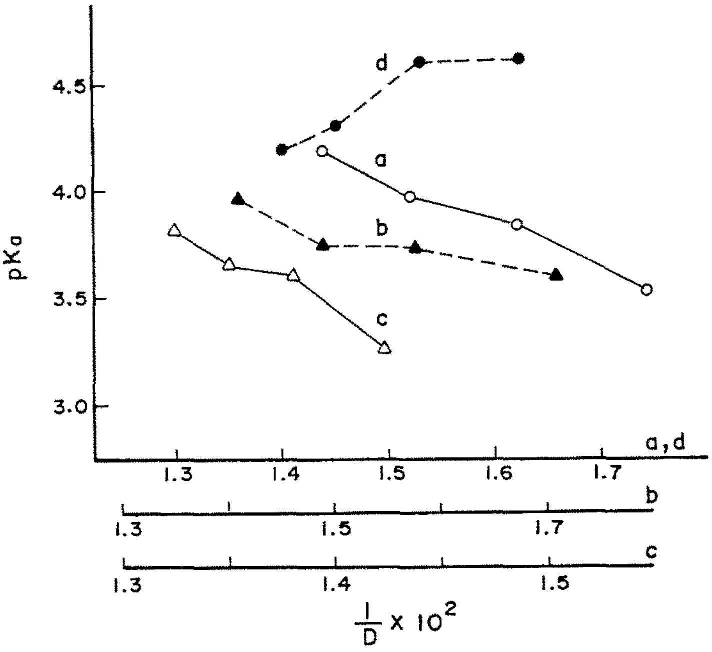

Fig. 1. $pK_a - 1/D$ relationship of 2,2′-bipyridyl in aquo-organic solvent mixtures. a – methanol; b – ethanol; c – *DMSO*; d – acetonitrile

not the case (Table 1, 2), therefore one can deduce that differences in stabilization of the free base of such compounds by donor hydrogen bond in partially aqueous media relative to that in pure one do not appear to be of much importance in the acid dissociation process of the investigated compounds.

Generally, it is recognized that properties of solvent such as dielectric constant, acidic or basic strengths play a major but not exclusive role. Other factors, such as stabilization of the different species existing in equilibrium through hydrogen bonding together with ion solvent interaction and dispersion forces play an important role on the acid dissociation of these compounds. Accordingly, the observed increase in the acid dissociation constant values of the investigated compounds as the amount of the co-organic amphiprotic or dipolar aprotic solvent *DMSO* in the aqueous media is increased, can be mainly ascribed to the high stabilization of the free base of each compound by dispersion forces rather than by hydrogen bonding in partially aqueous media. This dispersion interaction is established between the delocalized oscillator dipole of the free base and the localized oscillator dipole of the solvent. The stabilization of the free base by dispersion forces in partially aqueous media relative to those in pure ones is due to the fact that the effective density of dispersion centers of methanol or ethanol or *DMSO* is higher than that of water [18, 19]. Furthermore, the observed decrease in pK_a of the studied compounds as the amount of the organic solvent (alcohol or *DMSO*) in the medium is increased can be attributed also to the expected high stabilization of the proton by its interaction with organic solvent and water molecules in the mixtures than that with water molecules alone [13].

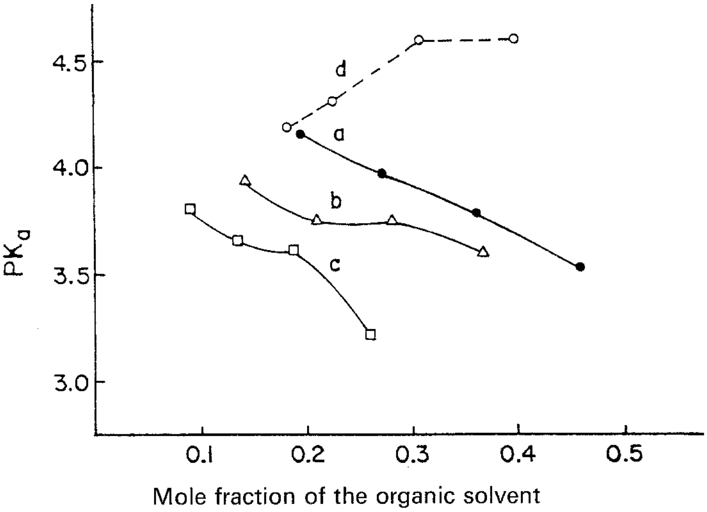

Fig. 2. Variation of the pK_a of 2,2′-bipyridyl with the mole fraction of the organic solvent in aqueous media. a – methanol; b – ethanol; c – *DMSO*; d – acetonitrile

Careful examination of the pK_a values of the four compounds investigated in the different methanol, ethanol, *DMSO*-water mixtures reveals the trend that in the presence of the same amount of the organic solvent in the medium, the pK_a varies with the nature of the co-organic solvent used according to the sequence: *DMSO* < ethanol < methanol. (cf. Fig. 2). However, this is expected as a result of the decrease in the solvent polarizability, going from *DMSO* to methanol within the above sequence [18, 19]. This behaviour can be considered as convincing evidence for the fact that the high stabilization of the free base of the heterocyclic diimines by dispersion forces and of the proton by its interaction with solvent molecules in partially aqueous media relative to that in pure aqueous one are the two important factors responsible for the observed decrease in pK_a of these compounds as the amount of co-organic solvent in the medium is increased.

Furthermore, the high basic character of *DMSO* will be reflected in the construction of a strong acceptor hydrogen bond from the protonated compound, thus facilitating the acid dissociation process of these compounds. Therefore one can suggest that changing the medium basicity by increasing addition of *DMSO* in the aqueous medium can be considered as an additional factor for the easier acid dissociation process of these compounds in presence of the dipolar-aprotic co-solvent *DMSO*.

Effect of Low Basic Aprotic Solvents

The results listed in Tables 1 and 2 reveal the behaviour that the acid dissociation constant values of the protonated form of each of the investigated compounds decreases as the amount of acetonitrile in the medium is increased (i.e. high pK_a). Though acetonitrile and methanol have nearly the same dielectric constant (36.0 and 32.6, respectively) as well as the two solvents have a comparable polarizability [13], the pK_a in acetonitrile- and in methanol-water mixtures of the same composition are different (Tables 1, 2). This behaviour can be considered as a further convincing evidence for the above reported conclusion that the electrostatic effect will have a relatively small influence on the acid dissociation process of the protonated form of the investigated compounds. Thus the observed increase in pK_a value as the proportion of acetonitrile in the medium is increased can be mainly attributed to the very low basic character of acetonitrile [20]. This reflects itself in a very poor hydrogen bond acceptor capability of acetonitrile (i.e. difficult acid dissociation of HB^+ as the amount of acetonitrile in the medium is increased). In conclusion, one can deduce that the basicity effect of acetonitrile (rather than other solvent effects) plays the major role in determining the acid dissociation constant value of the studied heterocyclic diimines in acetonitrile-water mixtures.

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Received December 17, 1991. Accepted July 7, 1992