

Acid dissociation equilibria of benzimidazole-2-carboxaldoxime in mixed solvents

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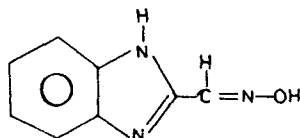
MS received 18 July 1983; revised 16 January 1984

Abstract. The acid dissociation constants of the benzimidazole-2-carboxaldoxime have been determined pH-metrically in different proportions of aqueous methanol, ethanol, isopropanol, acetone and dioxane. The influence of ionic strength, temperature and solvent on the acid dissociation equilibria of $-OH$ and $-NH=$ groups has been studied. A comparison of ΔH and ΔS terms in different aquo-organic media reveals that the positive ΔS is probably the main driving force in the acid dissociation processes of these groups. The effect of solvent was discussed in the light of dielectric constants, solvent basicity, hydrogen bonding and solute solvent interactions that operate in various aquo-organic media.

Keywords. Benzimidazole-2-carboxaldoxime; mixed solvents; dielectric constant; solvent basicity.

1. Introduction

The effect of solvent properties and solute-solvent interactions on equilibrium constants of acid dissociation processes is not well understood. Addition of organic solvent to water brings about a radical change in the properties of the medium. Thus the strength of the oxygenated acids (HA) becomes weaker when an organic solvent is added to water (Irving and Rossotti 1956; Shelke and Jahagirdar 1978; Chaudhury and Kole 1981a, b). Conversely nitrogenous bases (*i.e.* cationic acids BH^+) like anilines, pyridines and amines show a reverse trend and thus become stronger acids in aquo-organic media (Grunwald and Gutbezahl 1953; Harkins and Freiser 1955). Influence of ionic strength also revealed analogous trends on the acid dissociation equilibria of HA and BH^+ groups (Hanania and Irvine 1962). However, little work is reported on the effect of ionic strength, temperature and solvent on the acid dissociation equilibria of the compounds that contain both these groups. Hence the present study is aimed to investigate such aspects. Benzimidazole-2-carboxaldoxime [BAOX (scheme 1)] is



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chosen for this purpose, as it contains both a protonation centre ($-\overset{+}{N}H=$ group) and a dissociable ($-OH$) group.

2. Experimental

The acid dissociation constants were determined using Irving and Rossotti (1953, 1954) pH-titration technique (i) at 20°, 25°, 30° and 40° in 50% and 70% v/v aq. dioxane (ii) at $I = 0.03, 0.05, 0.10, 0.15, 0.20$ M ($NaClO_4$) in 50% v/v aq. dioxane at 30°; (iii) in 30, 40, 50, 60 and 70% v/v aqueous mixtures of dioxane, acetone, methanol, ethanol and isopropanol at 30°.

Owing to the solubility problem, titrations were not carried out below 30% (v/v) aquo-organic mixtures. The experimental details, including the ligand preparation, were described earlier (Omprakash *et al* 1981, 1982). The temperature was controlled to $\pm 0.05^\circ$ in all the titrations by circulating water from a high precision thermostat. (Toshniwal make).

3. Results and discussion

In the lower pH region, the ligand titration curve (pH vs volume of base) lies above the acid curve due to the basic property of the pyridyl (tertiary) nitrogen of benzimidazole ring to accept protons from strongly acid medium. However, in the higher pH region, the curve lies below the acid curve due to the release of $-OH$ protons. As indicated by \bar{n}_H values ($0.12 < \bar{n} < 1.96$) no dissociation of the imino (NH) proton of the imidazole ring was observed even up to pH 12.8. From the pH and \bar{n}_H data the values of pK_{OH} and pK_{NH} were evaluated by various computational techniques *viz* Bjerrum's half integral method, point-wise calculations, linear plots, least squares (Irving and Rossotti 1953) and Block and McIntyre (1953) methods. The values so obtained are consistent with each other. The deviations are within ± 0.01 pKa units.

3.1 Effect of ionic strength

A perusal of the data (table 1) indicates that the pK_{OH} values decrease while pK_{NH} increase on increasing ionic strength. This is in conformity with the observations made on typical weak acids and bases (cationic acids) (Shelke and Jahagirdar 1978; Hanania

Table 1. Acid dissociation constants of BAOX.

Ionic strength (M)	50% (v/v) aq.dioxane ^a		Temp. °C	50% (v/v) aq.dioxane ^b		70% (v/v) aq.dioxane ^b	
	pK_{NH}	pK_{OH}		pK_{NH}	pK_{OH}	pK_{NH}	pK_{OH}
0.00	3.26	11.08	20	3.71	11.36	3.43	12.34
0.03	3.36	10.98	25	3.53	11.10	3.31	12.08
0.05	3.41	10.92	30	3.45	10.83	3.15	11.82
0.10	3.45	10.83	40	3.20	10.34	2.91	11.33
0.15	3.49	10.78					
0.20	3.53	10.73					

$a = 30^\circ$; $b = 0.1$ M $NaClO_4$.

and Irvine 1962). In the acid dissociation reaction the $-OH$ group produces a negatively charged species from a neutral molecule (equation (1)), while a basic group ($-\overset{+}{N}=\overset{-}{O}$) produces a neutral molecule from a positively charged cationic species (equation 2).



Thus it can be inferred that as ionic strength of the medium increases the molecule tends to remain in ionic form *i.e.* L^- ion in the case of (1) and H_2L^+ ion in the case of (2). Linear plots are observed between \sqrt{I} and either pK_{NH} or pK_{OH} .

3.2 Effect of temperature

It is observed that the pK_{OH} and pK_{NH} values decrease with an increase in temperature suggesting that the dissociation reactions are favourable at higher temperatures. The thermodynamic parameters *viz* ΔG , ΔH and ΔS associated with the proton dissociation reactions are calculated utilizing the standard equations (Bell 1973) and are presented in table 2. The uncertainties in ΔH and ΔS are ± 0.46 kJ and 0.95 JK $^{-1}$ respectively. The positive values of free energy change (ΔG) suggest that the proton dissociation reactions are not spontaneous, while the positive enthalpy change (ΔH) shows the endothermic nature of these reactions. Further, the ΔH values are almost constant in both 50% and 70% (v/v) aqueous dioxane mixtures. This is expected because the strength of the proton-ligand bond is essentially the same in both these media (Harkins and Freiser 1955). A comparison of the ΔH and ΔS terms in 50% and 70% (v/v) dioxane reveals that it is the positive entropy change which is probably the main driving force in these dissociation processes. Therefore, the difference in ΔG (which is a measure of the extent of acid dissociation) may be due to varying degree of solute-solvent interactions in different aquo-organic media.

3.3 Effect of solvent

The influence of solvent on the acid-base equilibria is mainly interpreted in terms of electrostatic and nonelectrostatic effects *viz* dielectric constant of the medium structure and basicity of solvent, hydrogen bonding between solute and solvent molecule and other solute-solvent interactions. The latter effects depend on the nature of the solvent (Bates *et al* 1966; Rorabacher *et al* 1971). In the present study the pK_{OH} values increase

Table 2. Thermodynamic parameters associated with the acid dissociation equilibria of BAOX.

Thermodynamic parameter	v/v % dioxane	pK_{OH}	pK_{NH}
ΔG (30°)	50	62.8	20.0
kJ mol $^{-1}$	70	68.6	18.9
$\Delta H \pm 0.46$	50	89.8	45.9
kJ mol $^{-1}$	70	89.2	46.2
$\Delta S \pm 0.95$	50	89.8	85.4
J mol $^{-1}$ deg $^{-1}$	70	68.1	91.9

with an increase in the organic content of the solvent mixture. For all the solvent systems (table 3), plots of pK_{OH} against mole fraction (X_2) of organic solvent are linear (figure 1a, b). Plots of pK_{OH} against $1/\epsilon$ are also linear (figure 1c), except for aqueous dioxane which showed a curvature (figure 1d). In dioxane system the initial points (30, 40 and 50%) invariably fell on a straight line while the latter points corresponding to low dielectric constant ($\epsilon \leq 25$) deviate from it. A perusal of these results indicates that the acid dissociation equilibria in media of intermediate ($\epsilon > 32$) and high dielectric constant are primarily governed by the electrostatic effect. The deviations in low dielectric constant may be due to nonelectrostatic forces that operate in these media (dioxane) where a change in the structure of the solvent occurs (Frank and Evans 1945). Similar observations were made on a number of carboxylic and hydroxylic acids (Irving and Rossotti 1956; Shelke and Jahagirdar 1978).

The influence of solvent composition on the acid dissociation equilibria of the pyridyl (NH^+) group is less when compared to that of $-OH$ group. For example, on passing from 30% to 70% v/v methanol the pK_{NH} decreases by 0.24 only. No linear plots were obtained between pK_{NH} and either X_2 or $1/\epsilon$. Similar observations were

Table 3. Acid dissociation constants of BAOX in various aquo-organic media ($f = 0.1 M NaClO_4$; Temp. = 30°).

v/v	X_2	$100/\epsilon$	pK_{OH}	pK_{NH}
Methanol				
30	0.160	1.539	9.50	3.68
40	0.228	1.650	9.62	3.61
50	0.307	1.778	9.72	3.56
60	0.400	1.951	9.83	3.47
70	0.508	2.162	9.98	3.44
Ethanol				
30	0.116	1.604	9.86	3.66
40	0.170	1.758	9.97	3.55
50	0.235	1.951	10.13	3.53
60	0.315	2.198	10.38	3.45
70	0.416	2.516	10.61	3.38
Isopropanol				
30	0.092	1.695	9.94	3.60
40	0.136	1.905	10.10	3.53
50	0.190	2.193	10.20	3.50
60	0.261	2.597	10.42	3.42
70	0.354	3.185	10.71	3.36
Acetone				
30	0.095	1.606	10.05	3.56
40	0.140	1.767	10.18	3.52
50	0.196	1.970	10.30	3.48
60	0.268	2.255	10.48	3.37
70	0.362	2.646	10.76	3.28
Dioxane				
30	0.083	2.000	10.24	3.48
40	0.123	2.433	10.52	3.47
50	0.174	3.053	10.83	3.45
60	0.240	4.082	11.26	3.35
70	0.329	5.814	11.82	3.15

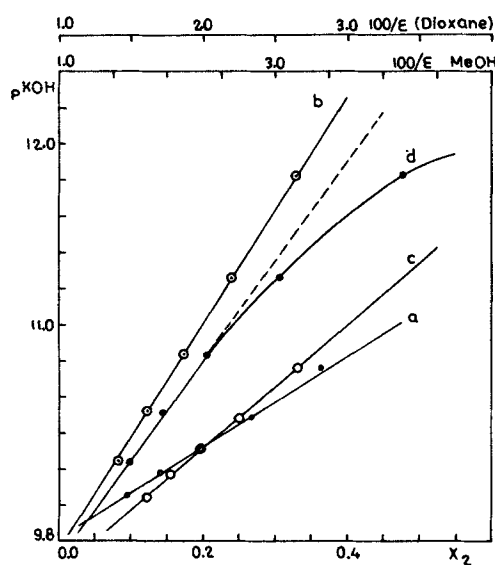


Figure 1. Plots of pK_{OH} vs X_2 (a) aq. methanol (b) aq. dioxane and plots of pK_{OH} vs $100/\epsilon$ (c) aq. methanol (d) aq. dioxane.

made with the acid dissociation equilibria of cationic acids like anilines and pyridines (Grunwald and Gutbezahl 1953; Harkins and Frieser 1955). Such a reversal of the solvent effect on the pK_{NH} values when compared to pK_{OH} can be explained in the light of solute-solvent interactions in mixed solvent systems (Bell and Dickenson 1949). An increase in the organic content of the solvent system results in a decrease in the dielectric constant of the medium. This will increase the electrostatic (ion-ion) interactions between a proton and a negatively charged oxygen atom to a greater extent than the ion-dipole interactions between the proton and the solvent. Thus as dielectric constant decreases, the pK_{OH} value increase for proton-ligand system containing O-H bonds. Conversely an increase in the organic content of the solvent is expected to increase the ion-dipole forces between a proton and a nitrogen atom in the ligand to a lesser extent than the ion-dipole forces between a proton and the more electronegative oxygen atom of the solvent. Therefore a decrease in the pK_{NH} value would be expected for compounds containing N-H bonds.

In a given percentage of mixed solvents, the order of pK_{OH} values are:

dioxane > acetone > isopropanol > ethanol > methanol.

An inverted order is found in pK_{NH} values. This order is in conformity with the sequence of $1/\epsilon$ in these mixed solvents (except for the position of acetone). The reversal of the position of acetone system may be due to its smaller proton solvation. Similar observations were made by Chaudhury and Kole (1981b).

Further, in a medium of isodielectric constant ($100/\epsilon = 1.95$), the order of pK_{OH} values (given in parenthesis) is:

$A - W(10.29) \geq D - W(10.22) > E - W(10.13) \geq I - W(10.07) > M - W(9.83)$.

This order is almost in accordance with the increased basicity of these solvents (Bell

1971; Braude 1948; Chaudhury and Kole 1981a). But in pK_{NH} , the values are almost constant suggesting that the structure and basicity of the solvent have little influence on the acid dissociation of cationic acid. Hydrogen bond formation between the solvent and the dissociating groups (*viz* OH and $\dot{N}H$) of BAOX, probably, play a significant role in determining their ionisation constants. The cationic acid ($\dot{N}H$ group in the present case) being weaker hydrogen bond donor, is little influenced by the solvent composition when compared to $-OH$ group. This is reflected in the order of pK_{OH} and pK_{NH} values given above. No further conclusions could be drawn on the influence of the "solvent nature" from these isodielectric constant studies, as an electrostatic effect caused by a change in dielectric constant of the medium is usually superimposed on the basicity of the solvent (Bates 1973).

4. Conclusions

A decrease in pK_{OH} values and an increase in pK_{NH} values on increasing ionic strength indicate that the molecule tends to remain in ionic form in a medium of high ionic strength. The positive entropy change is, probably, the main driving force in these acid dissociation equilibria. Though the dissociation processes are primarily governed by the electrostatic effects in media of high and intermediate dielectric constant, the present investigation serves to emphasize the considerable role of other factors like solvent basicity, hydrogen bonding and solute-solvent interactions.

Acknowledgement

The authors are grateful to CSIR, New Delhi for the award of fellowships to PE, PKR and KLOP.

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