

## Effect of dielectric constant of various mixed aqueous solvents on the proton-ligand and metal-ligand formation constants of N-methylisatin- $\beta$ -amidinohydrazone

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MS received 27 August 1984; revised 7 April 1986

**Abstract.** The proton-ligand formation constant of N-methylisatin- $\beta$ -amidinohydrazone ( $\beta$ -MIAG) and the metal-ligand formation constant of its complexes with  $\text{UO}_2(\text{II})$ ,  $\text{Cu}(\text{II})$ ,  $\text{Ni}(\text{II})$ ,  $\text{Co}(\text{II})$ ,  $\text{Pb}(\text{II})$ ,  $\text{Zn}(\text{II})$ ,  $\text{Cd}(\text{II})$  and  $\text{Mn}(\text{II})$  have been determined at a definite ionic strength,  $\mu = 0.1 \text{ M NaClO}_4$ , and at temperature  $30 \pm 0.5^\circ\text{C}$ , in aqueous organic solvents of different compositions. The variance of  $pK_a$  and  $\log \beta_n$  with the inverse of the dielectric constant or the mole fraction of the solvent has also been studied. The  $pK_a$  and  $\log \beta_n$  increases with the decrease of dielectric constant and the increase of the mole fraction of organic solvent of the media. In all the systems, the order of  $\log \beta_n$  values of  $\text{M}(\text{II})$ - $\beta$ -MIAG chelates is in accordance with Irving-William's series.

**Keywords.** Potentiometric determination; formation constants; N-methylisatin- $\beta$ -amidinohydrazone; dielectric constant of solvents.

### 1. Introduction

Derivatives of isatin and N-methylisatin are known to possess pharmacological activity. They act as central nervous system depressants and are used for the prevention of small pox etc. (Lozyuk 1974). The antimicrobial, antineoplastic, antihypotensive, analgesic, anti-inflammatory and cysticidal activity of isatin derivatives are well-known (Verma and Khan 1978). However, perusal of the literature reveals that no analytical work has been done on isatin and its derivatives. Hence, we have chosen N-methylisatin- $\beta$ -amidinohydrazone as a ligand to study its interaction with bivalent metal ions.

### 2. Experimental

#### 2.1 Instruments

A digital pH-meter (ECIL Model, pH-5651) with a single glass-calomel electrode assembly was used for pH measurements. It was standardised with suitable buffers before performing the titrations.

Constant temperature was maintained (to an accuracy of  $\pm 0.5^\circ\text{C}$ ) by using an

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MLW, West Germany, NEB type thermostat. Presaturated nitrogen was passed through the solution during the titration. The pH values in aquo-organic mixtures were corrected using the method of Van Uitert and Haas (1953) and volume corrections were applied by the method of Rao and Mathur (1969).

## 2.2 Reagents

N-methylisatin- $\beta$ -amidinohydrazone ( $\beta$ -MIAG) was prepared by refluxing equimolar quantities of N-methylisatin and aminoguanidine nitrate in alcohol. Its purity was further checked by IR, elemental analysis and TLC, m.p. 210–211°C. The solution of the ligand was prepared in freshly distilled dioxan. All the metal ion solutions were prepared from AR, (BDH) samples of the corresponding nitrates or sulphates and were standardised by conventional methods. Sodium perchlorate (Riedel) was used to keep the ionic strength constant. A 0.05 M solution of tetramethyl ammonium hydroxide (TMAH) (E Merck) was used as titrant. It was standardised with a standard solution of oxalic acid. The dioxan used was purified by refluxing with sodium metal for 24 hr and was freshly distilled over sodium before use. All other chemicals used were of reagent grade.

## 2.3 pH-titration procedure

The method of Bjerrum (1947) as modified by Irving and Rossotti (1953) was used to determine  $\bar{n}$  and  $pL$  values. The experimental procedure involved potentiometric titrations of the following solutions against 0.05 M TMAH in various aquo-organic media, at 0.1 M NaClO<sub>4</sub> ionic strength and 30 ± 0.5°C.

- (i) HClO<sub>4</sub> ( $1.5 \times 10^{-3}$  M)
- (ii) HClO<sub>4</sub> ( $1.5 \times 10^{-3}$  M) +  $\beta$ -MIAG ( $2.5 \times 10^{-3}$  M)
- (iii) HClO<sub>4</sub> ( $1.5 \times 10^{-3}$  M) +  $\beta$ -MIAG ( $2.5 \times 10^{-3}$  M) +  $M^{2+}$  ( $0.5 \times 10^{-3}$  M)

These titrations have been repeated for  $\beta$ -MIAG in different aquo-organic solvents (50, 60, 75% v/v dioxan–water, 75% v/v acetone–water and 75% v/v alcohol–water) in order to determine the variation of its  $pK_a$  and the stability of its metal complexes with change of dielectric constant and the mole fraction of the organic solvent.

## 3. Results and discussion

The parameters  $\bar{n}_A$ , the average number of protons bound per free ligand ion,  $\bar{n}$ , the average number of ligand bound per metal ion, and  $pL$ , the free ligand exponent were determined by the expressions described by Irving-Rossotti, in order to evaluate the  $pK_a$  of the ligand and the metal ligand stability constants,  $\log \beta_n$ . The stability constants were computed on an IBM 360 FORTRAN IV computer using a weighted least-squares program patterned after that of Sullivan *et al* (1959). The  $\beta_n$  values were initially approximated from the data ( $\bar{n}$ ,  $pL$ ) with the weight factor being unity, second approximations to the  $\beta_n$  values were then calculated by attaching to them appropriate weight factors, computed from the first set of  $\beta_n$  values, and the process was repeated until successive cycles gave a change of less than one part per thousand in each  $\beta_n$ .

The weighted least-squares treatment determines that set of  $\beta_n$  values, which make the function

$$U\left\{ U = \sum_{n=0}^N (y - x - nz)\beta_n x^n \right\}$$

nearest to zero, by minimizing

$$S\left\{ S = \sum_{i=1}^I U^2(x_i, y_i, z_i) \right\},$$

with respect to variation in  $\beta_n$ .

$S_{\min}$  has the same statistical distribution as  $\chi^2$  with  $K$  degrees of freedom, and with weight defined in accordance with Rydberg and Sullivan (1959). The dissociation constant  $pK_a$  and the stability constants of the metal complexes in various concentrations of organic solvents are given in tables 1 and 2. In 75% v/v organic solvent compositions, the sequence of  $1/\epsilon$  values is

dioxan–water > acetone–water > ethanol–water.

However, for the same v/v compositions, the  $pK_a$  values are in the sequence

acetone–water > dioxan–water > ethanol–water.

This indicates that the sequence does not follow the order of dielectric constants of the media.

In a mixed aqueous solvent the proton-ligand formation constant may be influenced by different solvent characteristics. These effects can be due to:

- (1) dielectric constant of the mixed solvents;
- (2) change of the hydrogen-bonding in water in the presence of organic solvents;
- (3) proton solvation of the organic solvent.

(1) Bates *et al* (1966) and Rorabacher *et al* (1971) have explained the change of  $\log K_H$  with solvent composition considering both electrostatic and non-electrostatic effects. They have concluded that the non-electrostatic phenomenon becomes increasingly important in solvents containing the organic solvent (OS) in more than 50% concentration.

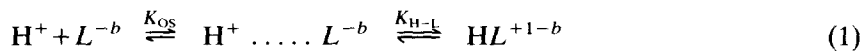
**Table 1.** Dissociation constants i.e.  $pK_a$  of  $\beta$ -MIAG in mixed aqueous solvents at  $30 \pm 0.5^\circ\text{C}$  and 0.1 M  $\text{NaClO}_4$  ionic strength.

Solvent composition (% v/v)	Mole fraction	Reciprocal of dielectric constant ( $1/\epsilon$ )	$pK_a$
Dioxan–water			
50	0.174	0.0293	7.95
60	0.240	0.0388	8.07
75	0.388	0.0699	8.52
Acetone–water			
75	0.422	0.0290	8.65
Alcohol–water			
75	0.479	0.0272	7.69

**Table 2.** Stability constant of bivalent metal complexes of  $\beta$ -MIAG in different mixed aqueous solvents at  $30 \pm 0.5^\circ\text{C}$  and 0.1 M  $\text{NaClO}_4$  ionic strength.

System	Stability constant	Solvent composition (% v/v)				
		Dioxan-water			Acetone-water	Alcohol-water
		50	60	75	75	75
$\text{UO}_2(\text{II})$ - $\beta$ -MIAG	$\log K_1$	7.008	7.206	7.819	7.571	7.251
	$\log K_2$	6.279	6.527	6.664	6.398	6.566
	$S_{\min}$	0.13533	0.11934	0.14215	0.15108	0.11219
$\text{Cu}(\text{II})$ - $\beta$ -MIAG	$\log K_1$	6.815	7.158	7.795	7.395	7.112
	$\log K_2$	5.413	5.759	6.360	6.272	5.978
	$S_{\min}$	0.02101	0.05244	0.36559	0.28168	0.26277
$\text{Ni}(\text{II})$ - $\beta$ -MIAG	$\log K_1$	5.847	6.394	7.140	6.745	6.454
	$\log K_2$	5.159	5.729	6.380	6.061	5.771
	$S_{\min}$	0.05705	0.04840	0.06901	0.05541	0.05421
$\text{Pb}(\text{II})$ - $\beta$ -MIAG	$\log K_1$	5.533	5.801	6.502	5.948	5.626
	$\log K_2$	4.225	4.540	5.240	4.777	4.458
	$S_{\min}$	0.04152	0.03981	0.04567	0.10963	0.10223
$\text{Co}(\text{II})$ - $\beta$ -MIAG	$\log K_1$	5.303	5.620	6.134	5.852	5.654
	$\log K_2$	4.135	4.184	5.044	4.765	4.241
	$S_{\min}$	0.04584	0.03665	0.11028	0.10894	0.02253
$\text{Zn}(\text{II})$ - $\beta$ -MIAG	$\log K_1$	5.296	5.459	6.127	5.831	5.509
	$\log K_2$	3.600	3.773	4.458	4.157	3.823
	$S_{\min}$	0.02857	0.03314	0.04526	0.04164	0.03479
$\text{Cd}(\text{II})$ - $\beta$ -MIAG	$\log K_1$	4.463	4.638	5.171	4.873	4.536
	$\log K_2$	3.380	3.463	3.750	3.448	3.388
	$S_{\min}$	0.00957	0.00776	0.01153	0.00984	0.00849
$\text{Mn}(\text{II})$ - $\beta$ -MIAG	$\log K_1$	4.189	4.405	4.846	4.548	4.506
	$S_{\min}$	0.02756	0.00234	0.10342	0.01331	0.00232

Protonation is viewed (Rorabacher *et al* 1971) as a two-step process,



solvent separated ion pair

$$\text{where, } K_{\text{H}} = K_{\text{OS}} \cdot K_{\text{H-L}}. \quad (2)$$

The values of  $K_{\text{OS}}$ , representing the diffusion controlled equilibrium constant for ion pair formation, can be calculated from Fuoss' (1958) equation.

$$K_{\text{OS}} = (4/3)\pi a^3 N_A 10^{-3} \exp [-(Z_{\text{H}} Z_{\text{L}} e_0^2)/\epsilon a k T] \quad (3)$$

where,  $a$  = distance of closest approach between the solvated proton and base in the ion pair. Other terms have their usual significance.

The term  $K_{\text{H-L}}$  in (2) represents the proton jump equilibrium occurring within the ion pair, presumably a non-electrostatic term dependent primarily on the relative basicity of the solvent and the base with a contribution from the nature and orientation of the solvent molecules separating the solvated proton and base species in the ion pair. It also appears that the non-electrostatic part of the

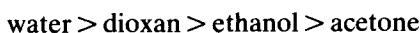
interaction is related to the proton acceptance property of the medium and the proton solvation of the organic solvent as discussed below. Taking the logarithm of (2) and including the Fuoss expression for  $K_{OS}$  we have

$$\log K_H = \log(4/3)\pi N_A 10^{-3} + 3 \log a + \log K_{H-L} - [Z_H Z_L q_0^2 / 2 \cdot 303kTa] \cdot (1/\epsilon) \quad (4)$$

Putting in the values of  $Z_L (= -1)$ , it is seen that with decreasing dielectric constant ( $\epsilon$ ) of the medium,  $\log K_H$  increases.

(2) According to Braude and Stern (1948), the tetrahedral lattice structure of water gradually breaks down with the addition of organic solvent, and owing to the denser packing and the smaller extent of hydrogen-bonding between water molecules, the stability of the hydroxonium ion increases and the proton-donating property of the medium falls. This may imply that the proton-accepting property of the solvent increases. It is also said that the H-bonded structure is less prevalent in pure ethanol in comparison of water and largely absent in pure acetone and pure dioxan. Gergely and Kiss (1977) have indicated that the dioxan molecules progressively break down the H-bonded structure of water, whereas ethanol can form H-bonded association with water. Hence, it is expected that the extent of H-bonding in ethanol-water is greater than that in dioxan-water or in acetone-water.

(3) Protonation of the organic solvent: When the amount of organic solvent becomes sufficiently large in a water-organic mixture, the proton solvation of the organic solvent molecules takes place. Braude (1948) has reported that the basicities of the pure solvent molecules decrease in the following order:



Thus the proton solvation of pure acetone is the least.

Effects (2) and (3) depend upon the concentration of the mixed aqueous media and they may be counteracting with respect to the proton acceptance property of the media. The more a solvent accepts protons the more the ligand acid is dissociated. Thus the  $pK_a$  will tend to decrease.

The foregoing solvent effects influence the  $pK_a$  of the ligand conjugate acid in the following manner:

- (a) With increase of solvent dielectric constant  $pK_a$  of the ligand decreases and vice-versa.
- (b) On decreasing the extent of hydrogen bonding in water by the organic solvent, the proton accepting property of water increases. Hence,  $pK_a$  of the ligand decreases.
- (c) Increasing proton solvation by the organic solvent decreases the  $pK_a$  of ligand and vice-versa.

The sequence for  $pK_a$  values in the different solvents is almost the same as that for dielectric constants of the solvents except in acetone which is in the top place (slightly higher than dioxan). Dioxan comes second, because it has the lowest dielectric constant but has greater proton solvation capacity and greater capacity to decrease H-bonding in water. Ethanol follows the sequence expected from its dielectric property. Moreover, ethanol has higher proton solvation than acetone.

In case of a dioxan–water mixture (50% v/v, to 75% v/v), the  $\log pK_a$  increases with the increase of dioxan content of the mixture (table 1). However, there is some deviation from linearity because both the effects (b) and (c) for dioxan lead to lowering of the  $pK_a$ .

The stability constants  $\log K_1$  and  $\log K_2$ , however, have some correlation with the  $1/\epsilon$  sequence in the different solvents, as proton solvation may not have any

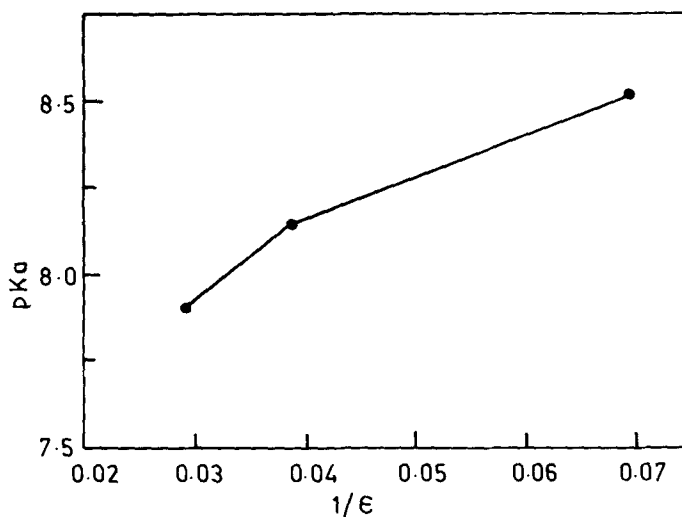


Figure 1. Plot of  $pK_a$  of  $\beta$ -MIAG vs.  $1/\epsilon$  for dioxan water.

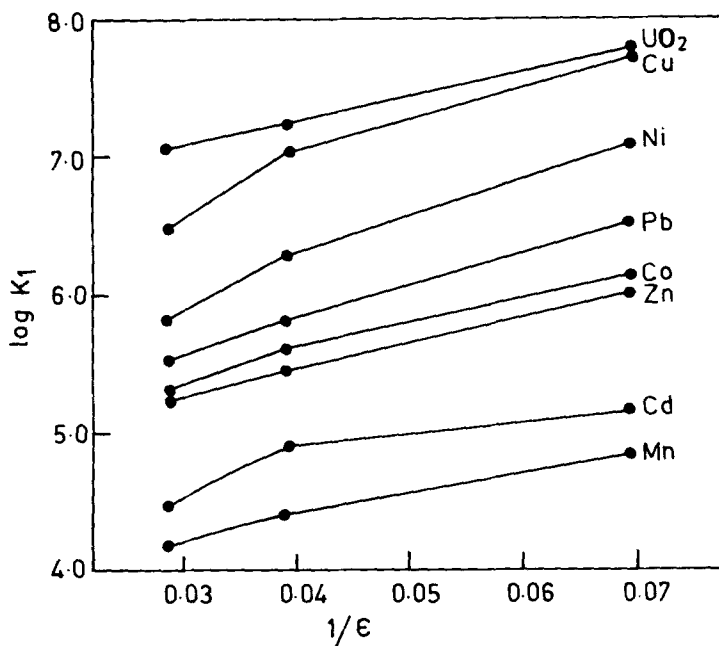


Figure 2. Plot of  $\log K_1$  of  $\beta$ -MIAG vs.  $1/\epsilon$  for dioxan water.

direct influence. The order of  $\log \beta_n$  has become almost similar to the  $1/\epsilon$  sequence (figures 1 and 2). Here again, it may be noted that the nature of the metal ions has little effect on the order. Comparison of the values of stability constants at 75% v/v shows the following sequence in the solvent mixtures for both  $\log K_1$  and  $\log K_2$  values:

dioxan–water > acetone–water > ethanol–water.

### Acknowledgement

One of the authors (KS) is thankful to CSIR, New Delhi, for financial assistance.

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