Potentiometric and Thermodynamic Studies of 4-Sulfamethoxazoleazo-3-methyl-2-pyrazolin-5-one and its Metal Complexes

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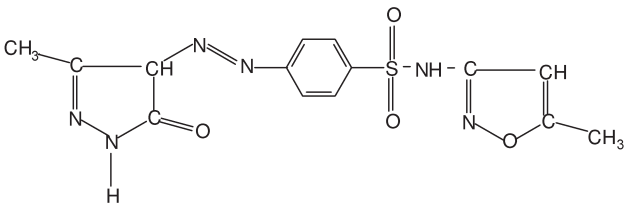
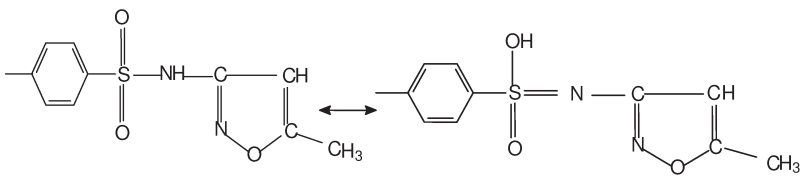
The dissociation constant of 4-sulfamethoxazoleazo-3-methyl-2-pyrazolin-5-one and metal—ligand stability constants of its complexes with bivalent (Mn^{2+}, Co^{2+}, Ni^{2+}, and Cu^{2+}) metal ions have been determined potentiometrically in 0.1 M-KCl and 40 vol. % ethanol—water mixture. The order of the stability constants of the formed complexes decreases in the sequence Cu^{2+}, Ni^{2+}, Co^{2+}, Mn^{2+}. The effect of temperature was studied and the corresponding thermodynamic parameters (ΔG, ΔH, and ΔS) were derived and discussed. The dissociation process is nonspontaneous, endothermic and entropically unfavourable. The formation of the metal complexes has been found to be spontaneous, endothermic, and entropically favourable.

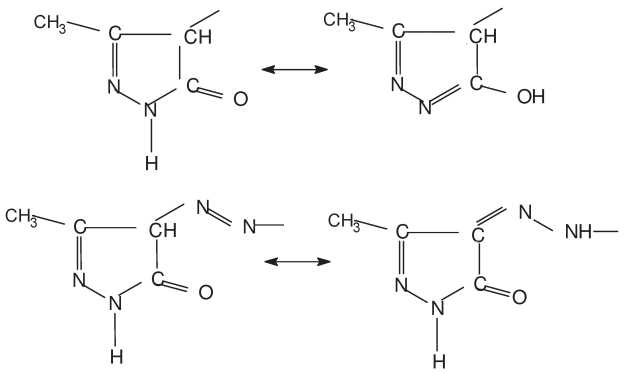
Azo compounds based on pyrazolone play a central role as chelating agents for a large number of metal ions. They form a stable six-membered ring after complexation with the metal ions and can also be used as analytical reagents [1]. Pyrazolone derivatives have been used in treatment of cancer [2].

In continuation to the earlier works [3, 4] herein the synthesis of 4-sulfamethoxazoleazo-3-methyl-2-pyrazolin-5-one (H_2L) is reported. The dissociation and the stability constants of Mn^{2+}, Co^{2+}, Ni^{2+}, and Cu^{2+} complexes with H_2L were determined potentiometrically at different temperatures. Furthermore, the corresponding thermodynamic functions of dissociation and complexation are evaluated and discussed.



Three types of tautomerism can be suggested as follows





The numbers of protons associated with the compound H_2L at different pH values, $\bar{n}_A$, were calculated from the titration curves of the acid in the absence and presence of a ligand. Thus, the formation curves ($\bar{n}_A$ *vs.* pH) for the proton—ligand systems were constructed and found to extend between 0 and 2 in the $\bar{n}_A$ scale. This means that ligands have two ionizable protons (the hydrogen ions of the hydroxyl group in the pyrazolone moiety (pK_{a2}) and sulfonamide group (pK_{a1})). It can be seen that for the same volume of NaOH added the ligand titration curves had a lower pH value than the acid titration curve. The displacement of a ligand titration curve along the volume axis with respect to the acid titration curve is an indication of proton dissociation. The proton-ligand stability constants (Table 1) were calculated using the method of *Irving* and *Rossotti* [5].

Table 1. Thermodynamic Functions for the Dissociation of H_2L in 40 vol. % Ethanol—Water Mixture and 0.1 M-KCl at Different Temperatures

T/K	Dissociation constant		Gibbs energy change kJ mol^{-1}		Enthalpy change kJ mol^{-1}		Entropy change J mol^{-1} K^{-1}	
	pK_{a1}	pK_{a2}	ΔG_1	ΔG_2	ΔH_1	ΔH_2	$-\Delta S_1$	$-\Delta S_2$
298	6.53	9.41	37.26	53.69			38.29	80.57
303	6.48	9.33	37.59	54.13			38.75	80.69
308	6.4	9.25	37.74	54.55	25.85	29.68	38.60	80.75
313	6.32	9.16	37.88	54.9			38.43	80.91
318	6.26	9.10	38.12	55.41			38.58	80.91

Table 2. Stepwise Stability Constants for ML and ML_2 Complexes of H_2L in 40 vol. % Ethanol—Water Mixture and 0.1 M-KCl at Different Temperatures

M^{n+}	298 K		303 K		308 K		313 K		318 K	
	$\log\{K_1\}$	$\log\{K_2\}$	$\log\{K_1\}$	$\log\{K_2\}$	$\log\{K_1\}$	$\log\{K_2\}$	$\log\{K_1\}$	$\log\{K_2\}$	$\log\{K_1\}$	$\log\{K_2\}$
Mn^{2+}	7.12	5.25	7.19	5.3	7.24	5.38	7.32	5.46	7.37	5.51
Co^{2+}	7.33	5.49	7.4	5.58	7.46	5.63	7.53	5.7	7.60	5.77
Ni^{2+}	7.39	5.55	7.48	5.63	7.52	5.70	7.6	5.78	7.66	5.84
Cu^{2+}	7.58	5.78	7.65	5.85	7.71	5.61	7.79	6.0	7.85	6.05

The formation curves for the metal complexes were obtained by plotting the average number of ligands attached per metal ions ($\bar{n}$) *vs.* the free ligand exponent (pL), according to *Irving* and *Rossotti* [6]. These curves were analyzed and the successive stability constants were determined using different computational methods [7, 8] which agree within 1 % error. Accordingly the average values are represented in Table 2.

The following general remarks can be pointed out:

i) The maximum value of $\bar{n}$ was ≈ 2 indicating the formation of 1:1 and 1:2 (n(metal):n(ligand)) complexes only.

ii) The metal ion solution used in the present study was very dilute (5×10^{-5} mol dm^{-3}), hence there was no possibility of formation of polynuclear complexes [9].

iii) The metal titration curves were displaced to the right-hand side of the ligand titration curves along the volume axis, indicating proton release upon complex formation of the metal ion with the ligand. The large decrease in pH for the metal titration curves relative to ligand titration curves points to the formation of strong metal complexes [10].

iv) In most cases, the colour of the solution after complex formation was observed to be different from the colour of the ligand at the same pH.

v) For the same ligand at constant temperature, the stability of the chelates decreases in the order Cu^{2+}, Ni^{2+}, Co^{2+}, Mn^{2+} [11].

The average dissociation constants (pK_a) for H_2L, as well as the stability constants ($\log\{K\}$) of its complexes with Mn^{2+}, Co^{2+}, Ni^{2+}, and Cu^{2+} have been evaluated at 298 K, 303 K, 308 K, 313 K, and 318 K (Tables 1 and 2). The enthalpy change (ΔH) for the dissociation and complexation processes was calculated from the slope of the plot pK_a or $\log\{K\}$ *vs.* $1/T$ (Figs. 1 and 2) using the graphical representation of van't Hoff equation

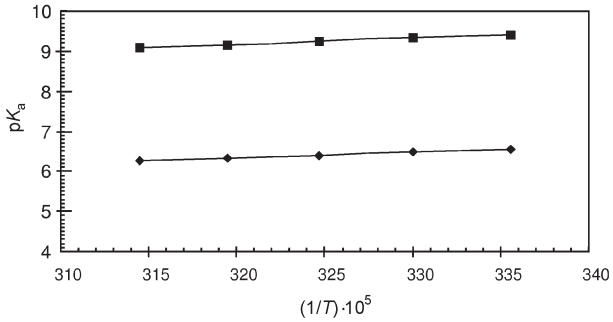


Fig. 1. Van't Hoff plot of pK_a of H_2L against $1/T$: ◆ pK_{a1} ■ pK_{a2}.

$$-2.303RT\log\{K\} = \Delta H - T\Delta S \qquad (1)$$

or

$$\log\{K\} = \frac{-\Delta H}{2.303R}\left(\frac{1}{T}\right) + \frac{\Delta S}{2.303R} \qquad (2)$$

From the Gibbs energy change ΔG and ΔH values one can deduce the entropy changes (ΔS) using the

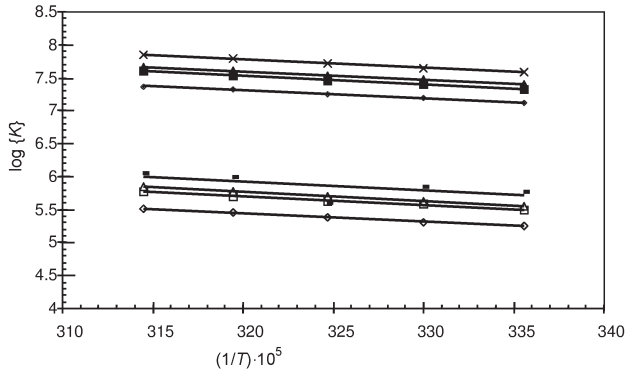


Fig. 2. Van't Hoff plots of $\log\{K_1\}$ and $\log\{K_2\}$ of M^{n+} complexes with H_2L against $1/T$. $\log\{K_1\}$: ◆ Mn^{++}, ■ Co^{++}, ▲ Ni^{++}, and × Cu^{++}. $\log\{K_2\}$: ◇ Mn^{++}, □ Co^{++}, △ Ni^{++}, and - Cu^{++}.

well known relationships (*3*) and (*4*)

$$\Delta G = -2.303\, RT \log\{K\} \qquad (3)$$

$$\Delta S = \frac{\Delta H - \Delta G}{T} \qquad (4)$$

where the gas constant $R = 8.314$ J K^{-1} mol^{-1}, K is dissociation constant for the ligand or stability constant of the complex, and T absolute temperature.

The thermodynamic parameters of the dissociation process of H_2L are recorded in Table 1. From these results the following conclusions can be made:

a) The pK_a values decrease with increasing temperature, *i.e.* the acidity of the ligands increases [3].

b) A positive value of ΔH indicates that the process is endothermic.

c) A large positive value of ΔG indicates that the dissociation process is not spontaneous.

d) The dissociation processes for H_2L have negative values of ΔS due to the increase order as a result of the solvation processes [12].

All the thermodynamic parameters of the stepwise stability constants of complexes are recorded in Table 3. It is known that the divalent metal ions exist in solution as octahedrally hydrated species and the obtained values of ΔH and ΔS can then be considered as the sum of two contributions: *a*) release of H_2O molecules, and *b*) metal—ligand bond formation.

Examination of these values shows that:

a) The stepwise stability constants ($\log\{K_1\}$ and $\log\{K_2\}$) for ligand complexes increase with increasing temperature, *i.e.* their stability constants increase with increasing the temperature.

b) The negative value of ΔG for the complexation process suggests the spontaneous nature of such process.

c) The ΔH values are positive, meaning that these processes are endothermic and favourable at higher temperature.

d) The ΔS values for the ligand complexes are positive, confirming that the complex formation is entropically favourable [13].

Table 3. Thermodynamic Functions for ML and ML_2 Complexes of H_2L in 40 vol. % Ethanol—Water Mixture in the Presence of 0.1 M-KCl

M^{n+}	T/K	Gibbs energy change		Enthalpy change		Entropy change	
		kJ mol^{-1}		kJ mol^{-1}		J mol^{-1} K^{-1}	
		$-\Delta G_1$	$-\Delta G_2$	ΔH_1	ΔH_2	ΔS_1	ΔS_2
Mn^{2+}	298	40.63	29.96	23.93	24.89	216.64	184.06
	303	41.71	30.75			216.63	183.63
	308	42.70	31.73			216.33	183.83
	313	73.87	32.72			216.61	184.06
	318	44.87	33.55			216.35	183.77
Co^{2+}	298	41.82	31.33	25.85	26.81	227.08	195.1
	303	42.93	32.37			226.49	195.13
	308	43.99	33.20			226.75	194.84
	313	45.13	34.16			226.77	194.79
	318	46.27	35.13			226.79	194.78
Ni^{2+}	298	42.17	31.76	25.85	27.86	228.26	199.43
	303	43.40	32.66			228.55	199.41
	308	44.35	33.61			227.92	199.25
	313	45.55	34.64			228.21	199.36
	318	46.64	35.56			227.96	199.12
Cu^{2+}	298	43.25	32.98	25.85	25.85	231.88	197.42
	303	44.38	33.94			231.78	197.33
	308	45.47	34.53			231.56	196.04
	313	46.69	35.96			231.76	197.48
	318	47.80	36.84			231.60	197.14

EXPERIMENTAL

Metal ion solutions (c = 0.0005 mol dm^{-3}) were prepared from Analar metal chlorides in bidistilled water and standardized with EDTA [14]. The ligand solutions (0.005 mol dm^{-3}) were prepared by dissolving the accurate mass of the solid in ethanol (Analar). Solutions of 0.005 M-HCl and 1 M-KCl were also prepared in bidistilled water. A carbonate-free sodium hydroxide solution in 40 vol. % ethanol—water mixture was used as titrant and standardized against oxalic acid (Analar).

H_2L was prepared [15, 16] by gradual addition of an aqueous solution of sodium nitrite (0.01 mol; 0.69 g) to a concentrated hydrochloric acid solution of sulfamethoxazole (0.01 mol; 1.72 g) with stirring and it was kept for about 20 min in the ice bath. The formed diazonium chloride solution was added gradually with stirring to cold solution of 3-methyl-2-pyrazolin-5-one (0.01 mol; 0.98 g) in 50 cm^3 of ethanol containing 5 g of sodium acetate. After dilution, the crude dye was collected by filtration and crystallized from ethanol, then dried in a vacuum desiccator over anhydrous $CaCl_2$. The purity was checked by elemental analyses, IR, and NMR spectra.

At the potentiometric measurements the apparatus, general conditions and methods of calculation were the same as in the previous works [3, 16]. The following mixtures were prepared and titrated potentiometrically at 298 K against standard 0.001 M-NaOH in 40 vol. % ethanol—water mixture

a) 5 cm^3 0.005 M-HCl + 5 cm^3 1 M-KCl + 20 cm^3 ethanol;

b) 5 cm^3 0.005 M-HCl + 5 cm^3 1 M-KCl + 15 cm^3 ethanol + 5 cm^3 0.005 M-ligand;

c) 5 cm^3 0.005 M-HCl + 5 cm^3 1 M-KCl + 15 cm^3 ethanol + 5 cm^3 0.005 M-ligand + 5 cm^3 0.0005 M-metal chloride.

For each mixture, the volume was made up to 50 cm^3 with bidistilled water before the titration. These titrations were repeated for temperatures of 303 K, 308 K, 313 K, and 318 K. A constant temperature was maintained at ± 0.05 K by using an ultrathermostat (Neslab 2 RTE 220). The pH-meter readings in 40 vol. % ethanol—water mixture are corrected according to the Van Uitert and Hass relation [15, 17].

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