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DISSOCIATION OF 5-NITROSO-2,4,6-TRIAMINO-PYRIMIDINE AND STABILITY OF ITS COMPLEXES WITH Co(II), Ni(II) AND Cu(II)

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ABSTRACT

The influence of ionic strength and temperature on the deprotonation process of 5-nitroso-2,4,6-triamino-pyrimidine as well as the stability of its complexes with Co(II), Ni(II) and Cu(II), in aqueous solution, has been studied by Bjerrum's method.

From data obtained, thermodynamic equilibrium constants for both dissociation and complexation processes have been calculated using the Debye–Hückel limit law and adjusting log K vs. $\sqrt{I}$ values at a parabolic equation by the least-squares method. Likewise, enthalpy and entropy changes for these reactions are reported.

INTRODUCTION

The study of interactions between organic bases with biological interest and metal ions has became an important subject of research in bioinorganic chemistry [1–5] due, fundamentally, to the chemotherapeutic properties that some metal–base complexes have shown [6–8].

By these reasons and following our already published works [9–12] about ionization processes of pyrimidine derivatives and stability of their metal complexes in solution, we account in this paper the influence of ionic strength and temperature on the deprotonation process of 5-nitroso-2,4,6-triamino-pyrimidine (TH) and the stability of its complexes with Co(II), Ni(II) and Cu(II) ions, in aqueous medium.

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EXPERIMENTAL

The ligand, 5-nitroso-2,4,6-triamino-pyrimidine (TH), was obtained as described in the literature [13]. All solutions were prepared in double-distilled carbon dioxide-free water. Solutions of TH (8×10^{-4} M) were prepared by direct weighing from a pure sample and solutions of Co(II), Ni(II) and Cu(II) nitrates were prepared and standardised. A standardised solution of sodium nitrate (1 M) was used to maintain the required ionic strength and a solution of carbonate-free sodium hydroxide (0.01 M) was prepared and standardised for acidimetric titrations.

The preparative methods to determine the ionization and stability constants were as follows:

(A) Ionization constants

In each case, an aqueous solution 4×10^{-4} M of TH (initial volume = 25 ml) was titrated against a standard alkali (0.01 M NaOH) after adjusting its ionic strength (0.01, 0.03, 0.06, 0.10, 0.20 M) and temperature (20, 25, 30 and 40°C).

(B) Stability constants

For this study, solutions (initial volume = 25 ml), in which $|M^{2+}| = 2 \times 10^{-4}$ M and $|M^{2+}|/|TH| = 1/2$, were titrated against a standard alkali (0.01 M NaOH) after adjusting the conditions of the medium: (i) at constant temperature (25°C) with ionic strength 0.01, 0.03, 0.06, 0.10 and 0.20 M and (ii) at constant ionic strength (0.10 M) and at 20, 25, 30 and 40°C.

Apparatus

A Crison-501 pH-meter, fitted with glass and calomel electrodes, was used for recording pH.

Both ionization and stability constants were calculated by Bjerrum's method [14]. In the case of stability constants, and according to the employed method, the ratio of metal to ligand concentration was kept at 1/2 in order to calculate the corresponding K_1 and K_2 values.

RESULTS AND DISCUSSION

In Table 1, experimental values of acidity constant of TH at different ionic strengths and temperatures are listed. These data indicate that, in aqueous solution, TH acts as a very weak acid, its dissociation constants being the smallest found by us for a pyrimidine derivative [10,15–20]. This

TABLE 1

Values of dissociation constant of TH at different ionic strengths and temperatures

T (°C)	pK_a				
I [a]	0.01	0.03	0.06	0.10	0.20
20	10.30	10.23	10.16	10.12	10.07
25	10.25	10.20	10.11	10.04	9.98
30	10.22	10.12	10.04	9.98	9.90
40	10.15	10.03	9.95	9.87	9.79

[a] I in mol l^{-1} $NaNO_3$.

table also shows that the acid character slowly increases with the increase of ionic strength and temperature of the medium. The first observation can be explained by the decrease of activity coefficients when the ionic strength increases and the second may be attributed to the increasing tendency of weak acids to dissociate when the temperature increases.

In order to obtain the corresponding thermodynamic ionization constants, pK_a values vs. $\sqrt{I}$ at each temperature have been plotted (Fig. 1).

Experimental points fitted well to straight lines, in the $I \leq 0.1$ M ionic strength range, from which, by extrapolation to zero ionic strength, we have obtained the corresponding thermodynamic pK_a^0 values. These and the corresponding free-energy change at each temperature are given in Table 2. The ΔG values indicate that the deprotonation of TH, in aqueous solution, is not a spontaneous process.

On the other hand, as is indicated by other authors [21], pK_a values fit the simple empirical equation

$$pK_a = a - b\sqrt{I} + cI \tag{1}$$

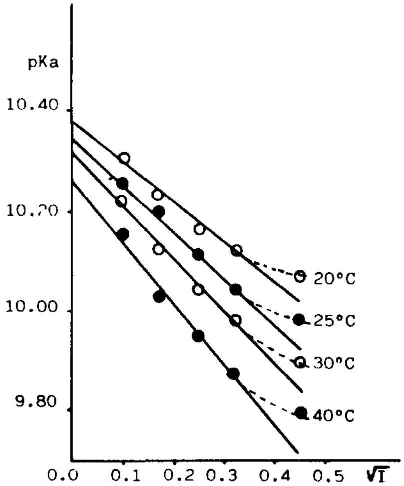

Fig. 1. Plot of pK_a vs. $\sqrt{I}$ at different temperatures.

TABLE 2

Thermodynamic acidity constant of TH at different temperatures

T (°C)	20	25	30	40
pK_a^0	10.38	10.36	10.32	10.27
r [a]	0.993	0.994	0.994	0.995
ΔG (kJ mol^{-1})	58.21	59.03	59.85	61.50

[a] r = correlation coefficient of regression straight line $pK_a = pK_a^0 - a\sqrt{I}\,(I \le 0.1$ M).

quite closely over the entire range of ionic strength employed. The adjustment of experimental data, at each temperature, to this parabolic equation by the least-squares method, has allowed to obtain for a, b and c coefficients the values given in Table 3. In this table, we have also listed the corresponding values of standard deviation (S_{yx}) of experimental data with respect to those calculated analytically by means of the former equation. This value can be interpreted as a measure of the accuracy of each fit.

In eqn. (1), it can easily be seen that the a parameter has to coincide theoretically with the thermodynamic pK_a^0 value. This can be confirmed by comparing the a values (Table 3) with the pK_a^0 values (Table 2), from which good agreement between both values can be observed.

In order to calculate the ΔH and ΔS values of dissociation process, at each ionic strength, pK_a values (Tables 1 and 2) vs. $1/T$ have been plotted (Fig. 2).

From these plots, and using the relation

$$pK_a = \frac{\Delta H}{2.303RT} - \frac{\Delta S}{2.303R}$$

we have obtained the ΔH and ΔS values given in Table 4.

Inspection of these data reveals that the ionization process of TH is an endothermic process, as could be expected for weak acid dissociation, while the entropy values are negative as a consequence of the hydration process produced during the ionization. Likewise, the enthalpy values increase with

TABLE 3

Adjustment of experimental pK_a values to empirical equation $pK_a = a - b\sqrt{I} + cI$, by the least-squares method

T (°C)	a	b	c	S_{yx} [a]
20	10.43	1.42	1.37	0.01
25	10.39	1.39	1.04	0.02
30	10.38	1.75	1.53	0.01
40	10.33	2.05	1.87	0.01

[a] S_{yx}: standard deviation of experimental pK_a values with respect to those calculated by the relation obtained.

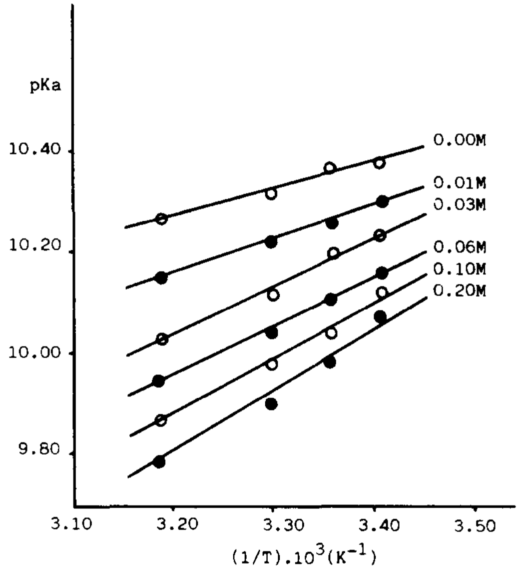

Fig. 2. Plot of pK_a vs. $1/T$ at different ionic strengths.

the increasing ionic strength which may be explained by the increase of the ionization of TH at the same time. The ΔS values show the same behaviour which is probably due to the growing difficulty for the hydration of produced ions, as a consequence of the competition with the ions of background electrolyte.

The stability constants of Co(II), Ni(II) and Cu(II) complexes of TH have been calculated, at several conditions, and are tabulated in Table 5.

In all cases, the stability constants decrease with the increase of ionic strength. This fact can be justified by the decreased tendency of the metal ion to interact with the ligand, since the negatively charged atmosphere around the cation is denser in salt solution, which prevents the close approach of ligands to the metal ion and, consequently, hampers the complexation process. This is in accordance with similar observations reported by Debye [22]. Likewise, it can be observed that log K values for

TABLE 4

ΔH (kJ mol^{-1}) and ΔS (J K^{-1} mol^{-1}) values for the ionization of TH at different ionic strengths

I (mol l^{-1} NaNO$_3$)	0.00	0.01	0.03	0.06	0.10	0.20
ΔH	9.95 [a]	12.94	17.78	19.07	21.64	24.53
$-\Delta S$	164.7 [a]	152.9	135.2	129.4	119.6	108.8
r(pK_a vs. $1/T$)	0.995	0.996	0.992	0.997	0.998	0.995

[a] Calculated from data of Table 2.

TABLE 5

Stability constants of TH complexes with Co(II), Ni(II) and Cu(II), at different temperatures and ionic strengths

Metal ion	I (mol l^{-1})	T (°C)	log K_1	log K_2	log β_2
Co(II)	0.01	25	6.74	5.86	12.60
	0.03	25	6.60	5.74	12.34
	0.06	25	6.50	5.66	12.16
	0.10	20	6.50	5.66	12.16
	0.10	25	6.40	5.58	11.98
	0.10	30	6.33	5.48	11.81
	0.10	40	6.18	5.31	11.49
	0.20	25	6.31	5.49	11.80
Ni(II)	0.01	25	7.35	6.51	13.86
	0.03	25	7.24	6.40	13.64
	0.06	25	7.15	6.33	13.48
	0.10	20	6.86	6.11	12.97
	0.10	25	7.06	6.24	13.30
	0.10	30	7.23	6.35	13.58
	0.10	40	7.56	6.58	14.14
	0.20	25	6.98	6.16	13.14
Cu(II)	0.01	25	8.94	8.60	17.54
	0.03	25	8.85	8.49	17.34
	0.06	25	8.76	8.39	17.15
	0.10	20	8.78	8.38	17.16
	0.10	25	8.71	8.30	17.01
	0.10	30	8.64	8.22	16.86
	0.10	40	8.50	8.07	16.57
	0.20	25	8.62	8.21	16.83

Co(II) and Cu(II) complexes decrease with a rise in temperature from 20 to 40°C. This suggests that the formation of these complexes is favoured at lower temperature, while the formation of Ni(II) complexes is favoured at higher temperatures.

The thermodynamic stability constants were obtained at 25°C by plotting log K_1 and log K_2 against $\sqrt{I}$ ($I \leq 0.1$ M) and extrapolating to zero ionic strength (Fig. 3). These values are reported in Table 6, which includes the corresponding ΔG for each complexation process.

In all cases, ΔG is negative which means that the complexation processes are spontaneous. The stability order of the complexes is in accordance with the Irving–Williams rule [23]. The values of stability constants are slightly higher than those found by other authors for complexes of Co(II), Ni(II) and Cu(II) with analogous pyrimidine derivatives [24,25].

In the same way that the acidity constants, stability constants also fitted the empirical equation

$$\log K = a - b\sqrt{I} + cI$$

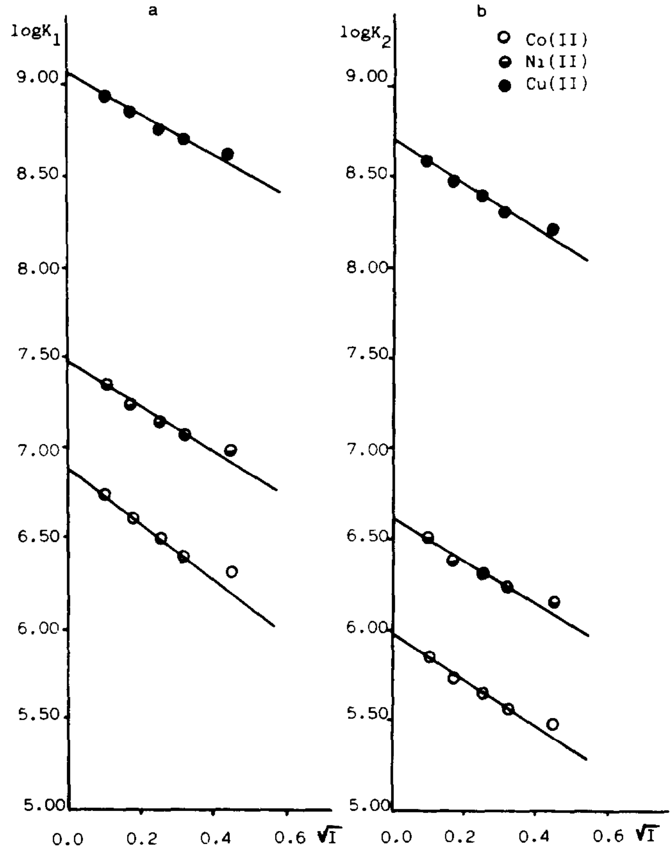

Fig. 3. Plots of (a) log K_1 and (b) log K_2 vs. $\sqrt{I}$ for TH–metal complexes at 25°C.

In Table 7, the values obtained by the least-squares method, for the three coefficients and S_{yx} are given. This allows reconstruction of experimental log K_1 and log K_2 against $\sqrt{I}$ plots over the entire range of ionic strength employed, with a standard deviation S_{yx}. In this case, a good concordance between a and log K^0 values is found.

Apparent ΔH and ΔS values for complexation processes have been

TABLE 6

Thermodynamic stability constants and free energy (kJ mol^{-1}) of TH–metal complexes at 25°C

Metal ion	log K_1^0	log K_2^0	log β_2^0	$-\Delta G_1$	$-\Delta G_2$	$-\Delta G$	r_1 [a]	r_2 [a]
Co(II)	6.88	5.98	12.86	39.24	34.10	73.34	0.999	0.995
Ni(II)	7.47	6.62	14.09	42.60	37.75	80.35	0.998	0.997
Cu(II)	9.05	8.73	17.78	51.61	49.79	101.40	0.996	0.998

[a] r_i: Correlation coefficient of regression straight line log K_i = log $K_i^0 - a\sqrt{I}$.

TABLE 7

Adjustment of experimental values of log K to empirical relation $\log K = a - b\sqrt{I} + cI$, by means of the least-squares method

	Co(II)/TH		Ni(II)/TH		Cu(II)/TH	
	log K_1	log K_2	log K_1	log K_2	log K_1	log K_2
a	6.97	6.04	7.54	6.68	9.09	8.80
b	2.51	1.98	2.06	1.84	1.64	2.10
c	2.31	1.69	1.79	1.51	1.32	1.76
S_{yx} [a]	0.01	0.01	0.01	0.02	0.01	0.01

[a] See Table 3.

calculated from log K vs. $1/T$ plots (Fig. 4). These values are tabulated in Table 8.

From this table, the exothermic character of the formation of Co(II) and

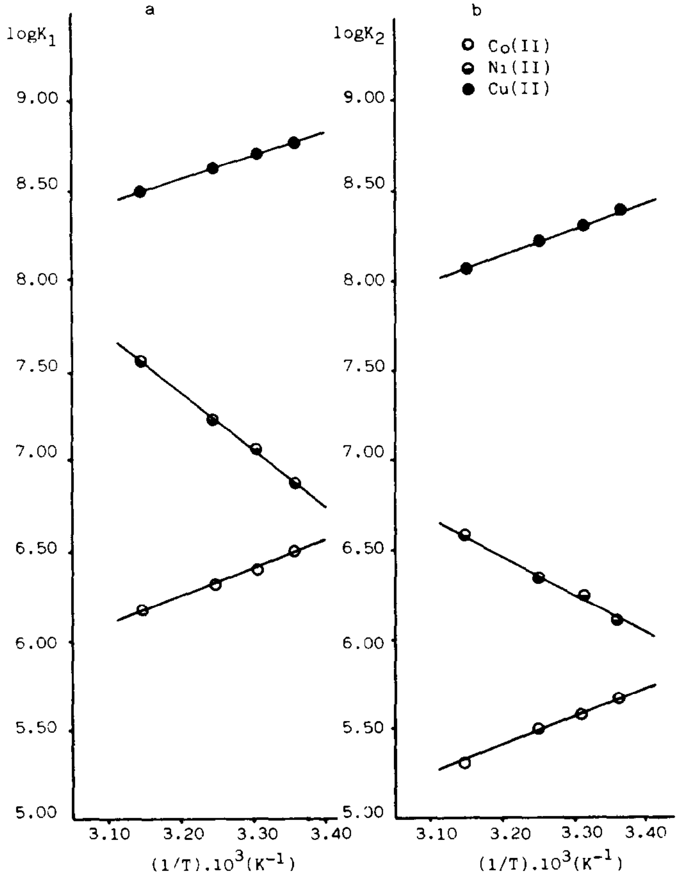

Fig. 4. Plots of (a) log K_1 and (b) log K_2 vs. $1/T$ for TH-metal complexes at 0.1 M ionic strength.

TABLE 8

Enthalpy (kJ mol^{-1}) and entropy (J mol^{-1} K^{-1}) changes of complexation processes at 0.1 M ionic strength

Metal ion	ΔH_1	ΔS_1	r_1 [a]	ΔH_2	ΔS_2	r_2 [a]
Co(II)	−27.7	29.8	0.999	−31.1	2.4	0.999
Ni(II)	61.1	339.8	1.000	41.0	257.0	1.000
Cu(II)	−24.6	84.0	1.000	−27.2	67.4	1.000

[a] r_i: Correlation coefficient of the regression straight line log K_i vs. $1/T$, obtained by the least-squares method.

Cu(II) complexes and the endothermic character of the formation of Ni(II) complexes can be observed. In the three cases, entropy values are positive but for Ni(II) complexes are much higher than for the other cases. For this reason and in spite of the positive value of ΔH, the formation of Ni(II) complexes is spontaneous at 25°C, these processes being favoured with a rise in temperature. The positive value of ΔS may be due to the increased disorder by the desolvation processes of metal ions and ligands, which are much greater than the increases in the order taking place in the complexation reactions.

Finally, the relationship between the values of thermodynamic stability constants (log K_1^0 and log K_2^0) of Co(II), Ni(II) and Cu(II) complexes and the ionization potential (IP) of the corresponding metal ion has been studied. This correlation is represented in the literature [26] by the following equation

$$\log K = \mathrm{p}(\mathrm{IP} - q)$$

where p and q are constants dependent only on the ligand, solvent and temperature of the medium and IP is the ionization potential of the metal ion (eV). As in other papers [11, 26 and references therein], log K^0 values have been converted into a dimensionless quantity by expressing concentrations in mole fractions. This means that, for water as solvent, K is 55 times greater than if it is expressed in l mol^{-1}. From the adjustment of log K_1 and log K_2 values versus IP at 25°C, by the least-squares method, the following values for p and q have been obtained

$$p_1 = 0.68 \quad q_1 = 4.44 \quad r = 0.997$$
$$p_2 = 0.87 \quad q_2 = 8.28 \quad r = 0.993$$

A comparison of these values with those reported in refs. 11 and 26 does not permit any conclusion to be drawn about the type of metal–ligand bond that takes place in these complexes. These anomalous values may be explained by steric effects that can be due to the structural differences seen in TH when compared with those reported in refs. 11 and 26.

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