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STABILITY AND THERMODYNAMIC PARAMETERS OF THIOPYRIMIDINES, 2-THIOXANTHINE AND THEIR COMPLEXES WITH Zn(II) AND Cd(II)

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ABSTRACT

The thermodynamic protonation constants of 4-amino-1,6-dihydro-2-methylthio-5-nitroso-6-oxo-pyrimidine (MTH), 4-amino-5-nitroso-6-oxo-1,2,3,6,-tetrahydro-2-thiopyrimidine (TANH) and 2-thioxanthine (TXH) in aqueous media at 25, 30, 40 and 50 ± 0.1°C, have been determined potentiometrically by Bjerrum and Robinson's methods. The ionic strength was maintained constant by using 0.1 M $NaNO_3$ as the supporting electrolyte.

The stability constants and thermodynamic functions for Zn(II) and Cd(II) complexes of MTH and TXH, at different ionic strengths and temperatures, have been calculated.

INTRODUCTION

Interactions between metal ions and pyrimidine and purine derivatives have attracted much attention in recent years [1–7], particulary after the discovery of the anti-neoplastic nature of some platinum(II) complexes [8–10]. On the other hand, complexes containing Ru(II), Ru(III) and Pt(II) ions show carcinostatic properties [11–13] and ions such as Zn(II) and Cd(II) have interesting importance in most of the biological processes involving enzymatic reactions [14].

Information about the structures of the metal complexes of pyrimidine and purine derivatives has been obtained by spectroscopic and crystallographic techniques [15,16] and some thermodynamic functions have been reported [17–19]. In this paper we account the results concerning the effect of temperature and ionic strength on the stability constants of some Zn(II) and Cd(II) complexes of several pyrimidine and purine derivatives, and the variations of acidity constants for these heterocyclic compounds.

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EXPERIMENTAL

4-Amino-1,6-dihydro-2-methylthio-5-nitroso-6-oxo-pyrimidine (MTH) and 4-amino-5-nitroso-6-oxo-1,2,3,6-tetrahydro-2-thiopyrimidine (TANH) were prepared as described in the literature [20–22]; 6-oxo-2-thiopurine(TXH) was obtained from Sigma Chemical Company.

All solutions were prepared in double-distilled carbon dioxide-free water. The solutions of MTH, TANH and TXH (2×10^{-4} M) were prepared by direct weighing from a pure sample, and solutions of zinc and cadmium were prepared and standardised. As usual, 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 titrations of free pyrimidine and purine bases were carried out at constant ionic strength (0.1 M) and at 25, 30, 40 and 50°C.

The study of the stabilities of the complexes was realized: (i) at constant temperature (25°C) with ionic strengths 0.01, 0.05, 0.1 and 0.2 M and (ii) at constant ionic strength (0.1 M) and at 25, 30, 40 and 50°C.

Apparatus

A Radiometer TTT-60 pH-meter, fitted with glass and calomel electrodes was used for recording pH.

The acid dissociation constants of MTH, TANH and TXH were calculated by Bjerrum and Robinson's methods [23,24], and the stability constants of Zn(II) and Cd(II) complexes by application of Bjerrum's method to the potentiometric titration curves of solutions having a 1 : 2 metal–ligand ratio.

RESULTS AND DISCUSSION

Table 1 shows experimental values of the acidity constants of pyrimidine (MTH) and (TANH) and purine (TXH) derivatives at different temperatures calculated by Bjerrum and Robinson's (in parentheses) methods [23,24]. Values found by both of these methods show an extraordinary concordance.

Inspection of the data in Table 1 reveals that acidity constants decrease with the increase in temperature. This trend can be satisfactorily explained by the decreasing tendency of weak acids to dissociate when the temperature increases.

The values of acidity constants for MTH and TANH are similar to those found for other analogous pyrimidine derivatives [25,26], whilst those for TXH are smaller than the xanthine ones [27] due to the shield produced by the C–S group on the hydrogen atom joined to N(3). Likewise, the data in Table 1 reveal that TANH is the strongest acid, and the acidity constants are in the order TANH > TXH > MTH.

TABLE 1

Acidity constants for MTH, TANH and TXH at different temperatures and 0.1 M ionic strength of $NaNO_3$

T(°C)	pK_1	$K_1 \times 10^7$	pK_2	$K_2 \times 10^{11}$
MTH				
25	6.47 (6.48)	3.39 (3.31)	10.32	(4.79)
30	6.42 (6.39)	3.80 (4.07)	10.26	(5.49)
40	6.31 (6.25)	4.90 (5.62)	10.13	(7.41)
50	6.18 (6.15)	6.61 (7.08)	10.01	(9.77)
	pK_1	$K_1 \times 10^5$	pK_2	$K_2 \times 10^{10}$
TANH				
25	4.96 (4.98)	1.10 (1.05)	10.10	(0.80)
30	4.92 (4.93)	1.20 (1.17)	9.95	(1.12)
40	4.85 (4.84)	1.41 (1.45)	9.73	(1.86)
50	4.78 (4.76)	1.66 (1.74)	9.55	(2.82)
	pK_1	$K_1 \times 10^6$	pK_2	$K_2 \times 10^{10}$
TXH				
25	6.02 (6.01)	0.95 (0.98)	9.64	(2.29)
30	5.97 (5.96)	1.07 (1.10)	9.59	(2.57)
40	5.86 (5.87)	1.38 (1.35)	9.48	(3.31)
50	5.77 (5.77)	1.70 (1.70)	9.32	(4.79)

In order to obtain the corresponding thermodynamic functions of the dissociation processes, $-\log K_1$ and $-\log K_2$ vs. $1/T$ have been plotted. Experimental points fitted well to straight lines in all cases when adjusted by the least-squares method. The calculated thermodynamic functions, which are summarized in Table 2, show that the enthalpy values are positive, as could be expected for weak acid dissociation, while the entropy values are negative, as a consequence of the increased order introduced during the solution process.

The stability constants of Zn(II) and Cd(II) complexes of MTH and TXH were calculated by application of Bjerrum's method. The values at different temperatures and ionic strengths are given in Table 3. In all cases, the stability constant values decrease with the increase in ionic strength. This fact can be justified by the decreased tendency of the metal ion to interact

TABLE 2

Apparent acid dissotiation enthalpies (kJ mol^{-1}) and entropies (J K^{-1} mol^{-1}) for MTH, TANH and TXH

Compound	ΔH_1	ΔH_2	ΔS_1	ΔS_2
MTH	22.1	23.1	−49.5	−119.3
TANH	12.5	37.6	−52.0	−65.9
TXH	18.4	22.4	−53.2	−108.8

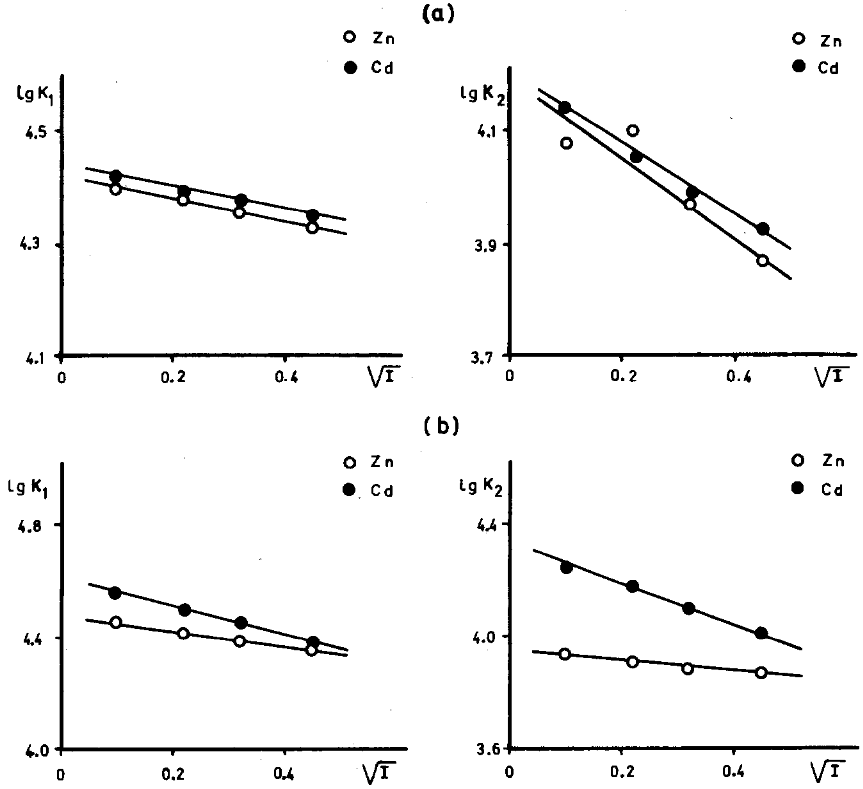

Fig. 1. log K_1 and log K_2 vs. $\sqrt{I}$ at constant temperature (25°C). (a) Complexes of MTH; (b) complexes of TXH.

TABLE 3

Stability constants for Zn(II) and Cd(II) complexes with MTH and TXH at different ionic strength and temperatures

I	T (°C)	System M^{2+}/MTH	log K_1	log K_2	log β_2	System M^{2+}/TXH	log K_1	log K_2	log β_2
0.01	25	Zn	4.40	4.08	8.48	Zn	4.46	3.94	8.40
0.05	25		4.38	4.10	8.48		4.42	3.91	8.33
0.1	25		4.36	3.97	8.33		4.39	3.89	8.28
0.2	25		4.33	3.87	8.20		4.36	3.88	8.24
0.1	30		4.33	3.96	8.29		4.35	3.87	8.22
0.1	40		4.29	3.94	8.33		4.30	3.83	8.13
0.1	50		4.24	3.91	8.15		4.23	3.80	8.03
0.01	25	Cd	4.42	4.15	8.57	Cd	4.57	4.25	8.83
0.05	25		4.39	4.06	8.45		4.50	4.18	8.68
0.1	25		4.38	3.99	8.37		4.46	4.10	8.56
0.2	25		4.35	3.93	8.28		4.38	4.02	8.40
0.1	30		4.36	3.98	8.44		4.43	4.04	8.47
0.1	40		4.30	3.92	8.22		4.37	3.94	8.41
0.1	50		4.25	3.88	8.13		4.33	3.88	8.21

TABLE 4

Thermodynamic constants and free energy values for Zn(II) and Cd(II) MTH and TXH complexes

Metal ion	log K_1	log K_2	log β_2	$-\Delta G_1$	$-\Delta G_2$	$-\Delta G$
MTH						
Zn(II)	4.42	4.18	8.60	25.12	23.75	48.87
Cd(II)	4.44	4.16	8.60	25.23	23.64	48.87
TXH						
Zn(II)	4.49	3.95	8.54	25.51	22.45	47.96
Cd(II)	4.62	4.32	8.94	26.25	24.55	50.80

with the ligand, since the negatively charged atmosphere around the cation is denser in salt solutions, which screens the interactions of the metal ions with the ligands, thus interfering with the complexation process. This is in accordance with similar observations reported by Debye–Hückel [28].

On the other hand, stability constant values show a decrease with a rise in temperature from 25 to 50°C. This suggests that the formation of Zn(II) and Cd(II) complexes is favoured at lower temperatures.

The thermodynamic stability constants were obtained at 25°C by plotting log K_1 and log K_2 against $\sqrt{I}$ (Fig. 1) and extrapolating to zero ionic strength. These values are reported in Table 4 with the corresponding energy change (ΔG) of the complexation processes. In all cases the complexation processes are spontaneous ($\Delta G < 0$).

The stability constants of the complexes are in the order Cd(II) > Zn(II). These results are in agreement with those obtained in the solid phase [29], where we have observed that coordination of MTH and TXH to Zn(II) and Cd(II) ions takes place through the sulphur atom and, therefore, in accordance with Pearson's Principle, between Cd(II) (soft acid) and Zn(II) (borderline acid) the Cd(II) ion prefers to bind to the sulphur atom (soft base).

Finally, we have calculated the enthalpy and entropy values associated

TABLE 5

Enthalpy (kJ mol^{-1}) and entropy (J K^{-1} mol^{-1}) values for Zn(II) and Cd(II) MTH and TXH complexes

Metal ion	ΔH_1	ΔH_2	ΔH	ΔS_1	ΔS_2	ΔS
MTH						
Zn(II)	−8.54	−4.31	−12.85	54.35	61.21	115.56
Cd(II)	−9.72	−8.48	−18.20	50.91	47.67	98.58
TXH						
Zn(II)	−10.01	−6.42	−16.43	49.77	52.63	102.40
Cd(II)	−9.64	−16.81	−26.45	52.63	21.74	74.37

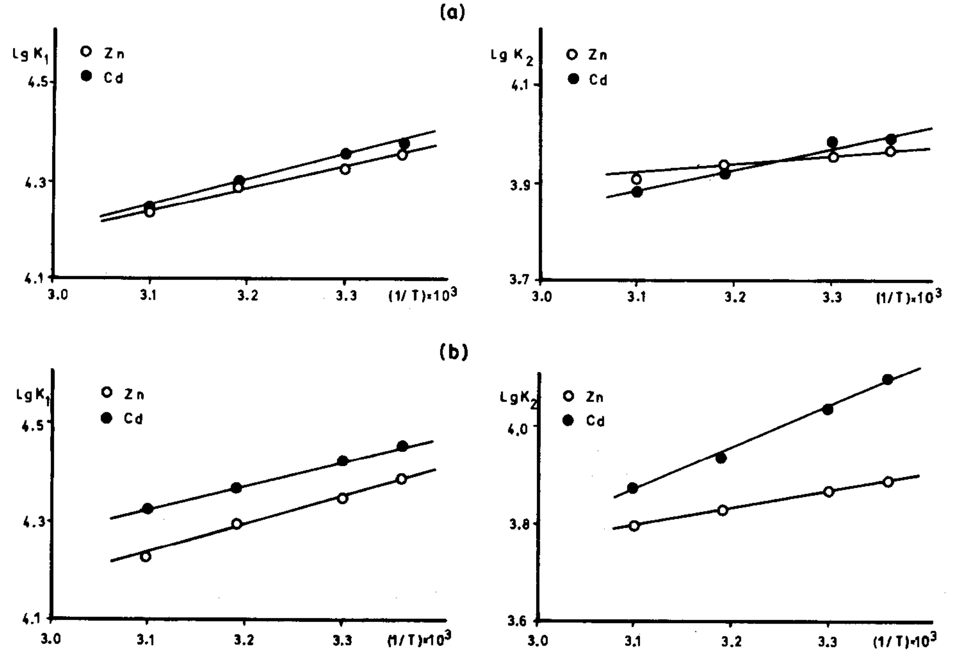

Fig. 2. log K_1 and log K_2 vs. T^{-1} at constant ionic strength (0.1 M). (a) Complexes of MTH; (b) complexes of TXH.

with the complex formation by plotting log K vs. $1/T$ (Fig. 2). These values are presented in Table 5. All enthalpy changes are negative and this indicates that complexation processes are exothermic; the entropy values are positive and this may be attributed to the release of solvated water molecules by the anion during complex formation and charge neutralization with the metal ion.

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