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THERMODYNAMICS OF THE COMPLEXATION OF Fe(II), Co(II), Ni(II), Cu(II), Zn(II) AND Cd(II) WITH 6,7-DIHYDRO-3(H)-METHYL-5-METHYLTHIO-7-OXO-VIC-TRIAZOLO(4,5-*d*)PYRIMIDINE

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ABSTRACT

The compound 6,7-dihydro-3(H)-6-methyl-5-methylthio-7-oxo-vic-triazolo(4,5-*d*)-pyrimidine, (LH), has been characterized spectroscopically (IR, ^{1}H-NMR and UV) and their acid behaviour studied at different ionic strengths and temperatures.

The formation constants of the complexes ML^+ and ML_2 (M = Fe(II), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II)) were obtained by the method of Chaberek and Martell and from these data, some of the thermodynamic functions for the processes were also calculated.

INTRODUCTION

The interest in the study of some different aspects concerning the complexes formed by certain transition metal ions with pyrimidine derivatives and 8-azapurine derivatives has led us to the thermodynamic study of some metal/ligand systems of the above type in aqueous media. Some of the results have been published recently [1,2].

As a continuation of these studies, in the present paper we show the results obtained from the thermodynamic study of the M(II)/ligand systems, where M(II) = Fe(II), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II), and the ligand was the compound 6,7-dihydro-3(H)-6-methyl-5-methylthio-7-oxo-vic-triazolo(4,5-*d*)pyrimidine (LH). It must be pointed out that in the system LH/Hg(II) the precipitation of a solid complex at extremely low values of the concentration, prevented us from its study.

As a previous step it was necessary to characterize spectroscopically (by IR, ^{1}H-NMR and UV spectroscopy) the compound used as ligand, and similarly the acidic character of LH was studied by Bjerrum's method [3]. Finally, we have obtained the stability constant values of the complexes of

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the type $(ML^-)^+$ and (ML_2^-) formed in all the M(II)/LH systems under different conditions (as we will see below), using the method of Chaberek and Martell [4].

EXPERIMENTAL

Reagents

The 8-azapurine derivative used as ligand in this work was synthesized as previously described by one of the authors [5]; the chemical analysis was realized in the Institut of Bioorganic Chemistry of C.S.I.C. (Barcelona).

All the inorganic chemicals used were analytical reagent grade. In all the solutions double-distilled carbon dioxide-free water was used as solvent. All the LH solutions used in the different steps of this work were prepared by diluting suitable volumes of a 10^{-3} solution of LH which was previously prepared by direct weight. Likewise, all the solutions containing the metal ion salts were prepared by diluting suitable volumes of 1.25×10^{-2} M (in the case of $ZnCl_2$ and $CdCl_2$) or 6.25×10^{-3} M (Mohr's salt, $CoCl_2$, $NiSO_4$ and $CuSO_4$) standardised solutions of the corresponding salt.

To maintain the ionic strength at adequate values, a standardised 0.1 M solution of KNO_3 was used.

Suitable standardised KOH solutions were also used in this work.

Apparatus and methods

The IR spectra of LH in solid state were obtained from KBr pellets (4000–200 cm^{-1} range) and polyethylene pellets (600–200 cm^{-1} range), using a Beckman 4250 spectrophotometer.

The ^{1}H-NMR spectrum of LH was obtained in a Hitachi Perkin-Elmer FT-NMR R-600 spectrometer, using DMSO-d_6 as solvent and TMS as internal standard, in the 0–20 ppm range.

The UV spectra of the ligand were obtained at various pH values (1.70–11.62 range) from a 5×10^{-5} M aqueous solution of the compound at 0.1 M ionic strength Na_2SO_4; a Spectronic 2000 spectrophotometer was used.

To study the acidic character of LH in aqueous media Bjerrum's method was used [3]. For this, 35 ml of a 5×10^{-4} M aqueous solution of LH were titrated against a 1.09×10^{-2} M standardised NaOH solution after adjusting the ionic strength and temperature at the appropriate values.

The stability constants K_1 and K_2 corresponding to the complexes formed in the systems M(II)/LH under study were calculated following the method of Chaberek and Martell. For this, solutions containing LH and M(II) in which the ratio of metal ions to ligand concentrations were kept at

1 : 2 (LH = 2.50×10^{-4} M), were titrated against a standardised 1.12×10^{-2} M KOH solution. In each solution the ionic strength and temperature were previously fixed at the appropriate values.

RESULTS AND DISCUSSION

As was stated before, the compound LH was synthesized by a method proposed by one of the authors [5]. The analytical data of LH are in good agreement with those calculated from the formula corresponding to the anhydrous LH. These data are: C, 36.60% (36.54); H, 3.52% (3.58); N, 35.27% (35.51); S, 16.31% (16.24), the values in parentheses being the calculated ones.

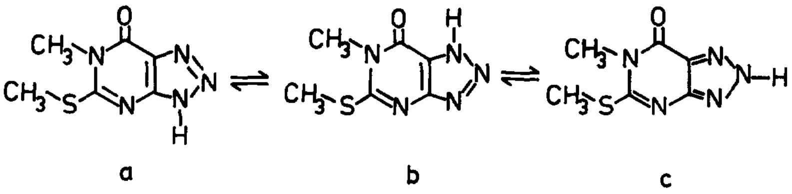
Given that no bibliographic data concerning this compound were found we have considered its spectral characterization to be necessary. The assignments of the bands in the IR spectrum of LH are summarized in Table 1. It must be pointed out that the assignment of the band at 1485 cm^{-1} to $\nu(N{=}N)$ stretching vibration was made on the basis that the only structural difference between the IR spectra of LH and its precursor 4,6-diamino-1-methyl-2-methylthio-6-oxo pyrimidine is the lack of such a band in the spectrum of the last compound [5]. The ^{1}H-NMR spectrum of LH shows the three expected singlets corresponding to the $S{-}CH_3$, $N_6{-}CH_3$ and the hydrogen atom, which are centered at 2.5, 3.4 and 10.0 ppm, respectively. The last δ value is higher than that of the hydrogen atom of the compound 6,7-dihydro-3(H)-6-methyl-5-methoxy-7-oxo-vic-triazolo-(4,5-*d*)-pyrimidine which has been reported in a recent paper [2]. This fact proves that the ionic

TABLE 1

IR spectral data of LH

ν (cm^{-1})	Intensity [a]	Assignments
3180	w	$\nu(NH)$
3120	m(br)	$\nu(NH)$
2960	w	$\nu(CH)$
2840	w	$\nu(CH)$
1670	s(br)	$\nu(C{=}O)$
1590	s	$\nu(C{=}N)$
1525	m	$\nu(C{=}C)$
1460	m	$\nu(N{=}N)$
1405	m	$\delta_{as}(C{-}H)$
1345	m	$\delta_s(C{-}H)$
1240	m	$\nu(C{-}N)$
1220	m	$\nu(C{-}N)$
660	m	$\nu(C{-}S)$

[a] w = weak; m = medium; s = strong; br = broad.



Scheme 1.

character of the bond between the hydrogen atom and the vic-triazolo cycle is stronger in the compound studied in the present paper. This fact is in accordance with the higher value of the thermodynamic dissociation constant, as we will see below.

The above IR and ^{1}H-NMR data, and especially the high value of the signal due to H acidic atom, are in accordance with the resonance between the structures shown in Scheme 1.

The UV spectrum of LH in aqueous solution shows three bands at 268 nm ($\epsilon = 9020$ l mol^{-1} cm^{-1}), 228 nm ($\epsilon = 12980$) and 205 nm ($\epsilon = 12370$). All the bands present relatively large values of the extinction coefficients, which is in accordance with probable $\pi \rightarrow \pi^*$ transitions. These assignments are in agreement with those made by several authors for the absorption spectra of purines and pyrimidines [6–8].

On the other hand, the UV spectral curves of LH at different pH values define one isosbestic point at 237 nm which corresponds to the displacement of the dissociation equilibrium $LH \rightleftarrows L^- + H^+$ [9].

The quantitative acidic behaviour of LH in aqueous solutions was studied by applying Bjerrum's method [3] to the potentiometric titration curves of LH solutions. These curves were obtained at variable T values (20, 25, 30, 40 and 50°C and 0.1 M ionic strength of KNO_3) and ionic strength (0.01; 0.02; 0.06 and 0.1 M of KNO_3 and $T = 25°C$). The corresponding K_c values for the process $LH \rightleftarrows L^- + H^+$ were calculated from the plots of $\bar{n}$ versus pH, by interpolating at $\bar{n} = 0.5$ (Table 2). These values are higher than those

TABLE 2

Ionization constants of LH at different ionic strengths and temperatures

I (mol l^{-1})	T (°C)	log K_c
0.01	25	−5.62
0.02	25	−5.58
0.06	25	−5.54
0.10	25	−5.49
0.10	20	−5.55
0.10	30	−5.42
0.10	40	−5.34
0.10	50	−5.26

corresponding to the compound 6,7-dihydro-3(H)-6-methyl-5-methoxy-7-oxo-vic-triazolo(4,5-*d*)pyrimidine [2], which is in accordance with the ^{1}H-NMR aforementioned data.

The K_c values obtained at different ionic strength define a straight slope positive line when they are plotted versus $\sqrt{I}$; the first feature is in accordance with the Debye–Hückel limiting equation for 1/1 electrolytes, $\log K_c = \log K_d + C_t\sqrt{I}$ [10]. On the other hand, the increase in K_c when I increases can be explained on the basis of the hindrances to proton–L^- interactions due to the negatively charged atmosphere around the protons.

The value of the thermodynamic dissociation constant (K_d) obtained from the experimental data is $K_d = 2.14 \times 10^{-6}$ mol l^{-1}. Likewise, the ΔG^0 value for the process under study was calculated using the equation $\Delta G = -2.303RT \log K_c$. This value is $\Delta G^0 = 32.33$ kJ mol^{-1}.

In Table 2 it can be seen also that K_c values increase on increasing T; this indicates that the dissociation process is endothermic. The plot of K_c vs. $1/T$ defines a straight line from which values of ΔH and ΔS (at ionic strength 0.1 M KNO_3) were calculated on the basis of the equation $\log K_c = -(\Delta H/2.303RT) + (\Delta S/2.303R)$. The values obtained were $\Delta H = 16.95$ kJ mol^{-1} and $\Delta S = -48.14$ J mol^{-1}. As was previously suggested [2] the negative value of ΔS suggests that the solvation process predominates over the dissociation one, under the experimental conditions used in this work.

The formation constants corresponding to the ligand stepwise addition processes to the central ion were calculated following the method proposed by Charberek and Martell [4]; K_c values of LH were used here. In accordance with this method the formation curves ($\bar{n}$ vs. pL^-) were obtained; all these curves level off at $\bar{n} = 1.9$, which indicates that in all the systems under study the 1/2 species are the highest formed in solution [11]. Nevertheless, in the system LH/Zn(II) at 50°C only the 1/1 complex was formed. By interpolating at $\bar{n} = 0.5$ and $\bar{n} = 1.5$, $\log K_1$ and $\log K_2$ values, respectively, were obtained. These values at different ionic strengths and temperatures are summarized in Table 3.

As should be expected, the values of K_1 and K_2 decrease when the ionic strength increases; this feature is similar to that found in other systems [1,2], which has been explained as a result of the hindrances to metal–ligand interactions caused by the solvation of the cation, which increases in intensity when the ionic strength increases.

In Fig. 1 $\log K_1$ and $\log K_2$ are plotted against $\sqrt{I}$; all the systems under study define straight lines. Therefore, we have used the Debye–Hückel limiting equation to calculate the thermodynamic stability constant values of both complexes 1/1 and 1/2. These values are shown in Table 4 together with the logarithm of the overall formation constant β_2.

The complexes of the type $[ML^-]^+$ have higher stability constant values in the case of Cu(II) and Ni(II), whereas just the opposite was verified in the four remaining cases; these results are similar to those found by other authors for the Cu(II), Ni(II) and Co(II) complexes of violuric acid, thio-2-violuric acid, monomethyl-violuric acid, monoethyl-violuric acid and 1,3-dimenthylvioluric acid [12], and to those found for Fe(II) complexes of 1,10-phenanthroline [13] and 2,4,6-tris(2-pyridyl)-1,3,5-triazine [14].

On the other hand, the values of K_1 and K_2 (Table 4) are in the same range as those found for the corresponding complexes of some 5-nitroso-6-oxo-pyrimidine derivatives [1,15–17] in which the ligands are probably bounded as chelates to the central ions via 5-NO and 6-oxo groups. Likewise, K_1 and K_2 values of Cu(II), Zn(II) and Cd(II) complexes are very

TABLE 3

Stability constants of the 1/1 and 1/2 complexes at different ionic strengths and temperatures

Metal ion	I (mol l^{-1})	T (°C)	log K_1	log K_2	log β_2
Fe(II)	0.01	25	4.05	4.35	8.40
	0.02	25	4.14	4.31	8.45
	0.06	25	4.02	4.28	8.30
	0.10	25	3.99	4.30	8.29
	0.10	20	4.06	4.34	8.40
	0.10	30	3.99	4.28	8.27
	0.10	40	3.98	4.31	8.29
	0.10	50	3.95	4.30	8.25
Co(II)	0.01	25	4.12	4.37	8.49
	0.02	25	4.11	4.40	8.51
	0.06	25	4.03	4.35	8.38
	0.10	25	3.97	4.35	8.32
	0.10	20	3.86	4.23	8.09
	0.10	30	3.83	4.23	8.06
	0.10	40	3.83	4.23	8.06
	0.10	50	3.79	4.22	8.01
Ni(II)	0.01	25	4.48	4.47	8.95
	0.02	25	4.42	4.46	8.88
	0.06	25	4.33	4.44	8.77
	0.10	25	4.22	4.42	8.64
	0.10	20	4.28	4.38	8.66
	0.10	30	4.14	4.36	8.50
	0.10	40	4.04	4.31	8.35
	0.10	50	4.00	4.30	8.30
Cu(II)	0.01	25	5.11	5.07	10.18
	0.02	25	5.04	4.97	10.01
	0.06	25	4.97	4.95	9.92
	0.10	25	4.95	4.94	9.89
	0.10	20	4.95	4.95	9.90
	0.10	30	4.90	4.90	9.80
	0.10	40	4.80	4.80	9.60
	0.10	50	4.75	4.76	9.51

TABLE 3 (continued)

Metal ion	I (mol l^{-1})	T (°C)	log K_1	log K_2	log β_2
Zn(II)	0.01	25	4.06	4.35	8.41
	0.02	25	4.05	4.33	8.38
	0.06	25	4.03	4.34	8.37
	0.10	25	4.03	4.33	8.36
	0.10	20	4.02	4.40	8.42
	0.10	30	3.90	4.30	8.20
	0.10	40	3.82	4.26	8.08
	0.10	50	3.63	–	–
Cd(II)	0.01	25	4.00	4.32	8.32
	0.02	25	3.97	4.29	8.26
	0.06	25	3.97	4.29	8.26
	0.10	25	3.95	4.27	8.22
	0.10	20	3.98	4.38	8.36
	0.10	30	4.00	4.33	8.33
	0.10	40	3.92	4.30	8.22
	0.10	50	3.83	4.27	8.10

similar to the corresponding ones of 6,7-dihydro-3(H)-6-methyl-5-methoxy-7-oxo-vic-triazolo(4,5-*d*)pyrimidine [2].

Given that the stability constants are in the order Fe(II) < Co(II) < Ni(II) < Cu(II) > Zn(II) > Cd(II) both the K_1 and K_2 values follow the Irving–Williams expected sequence for model compounds [11]. Moreover, the plots of log K_1 and log K_2 of Fe(II), Co(II), Ni(II) and Cu(II) complexes against the ionization potential (IP, in eV) of the metal ions define two straight lines (Fig. 2). This fact is in accordance with the equation log $K = p(\mathrm{IP} - q)$ [18,19] (where p and q are constants depending only on solvent and temperature), which implies that the coordination method is probably similar for the complexes of the four metal ions above mentioned [20].

The stability constant values for IIB group metal ions are in the order predicted by Van Panthaleon; but they do not follow the linear sequence defined by the remaining four cations (see Fig. 2); this probably means [20] that Zn(II) and Cd(II) are a type of complex different from those of Cu(II), Ni(II), Co(II) and Fe(II).

The ΔG standard values for all the complexation processes have been calculated on the basis of the relation $\Delta G = -2.303RT$ log K, all of them being negative (Table 4); this implies that all the processes under study are spontaneous.

As was said previously, the relation between log K_1 and log K_2 and the temperature (in the 20–50°C range) has been studied too. The corresponding log K_1 and log K_2 values given in Table 3 have been plotted vs. $1/T$ (Fig. 3). In all cases straight lines were defined from which, ΔH_i and ΔS_i for

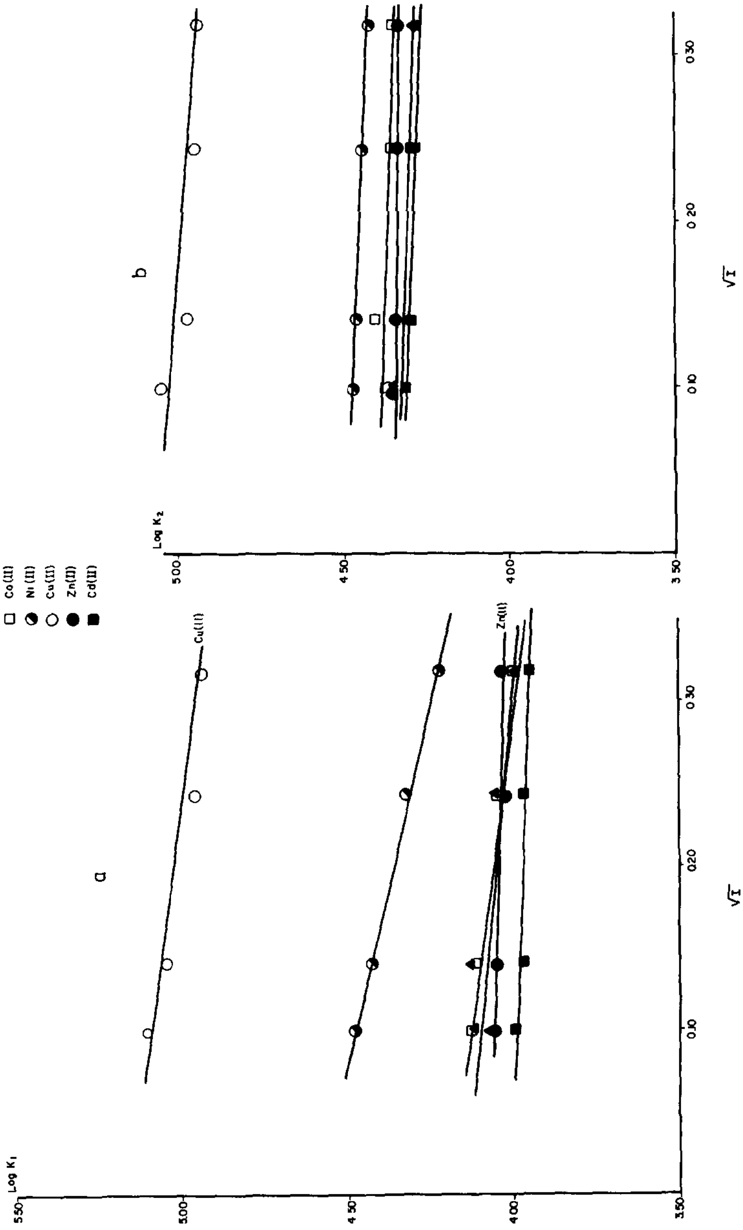


Fig. 1. Plots of (a) log K_1 and (b) log K_2 vs. I for the complexes at 25°C.

TABLE 4

Thermodynamic stability constants and free energy (in kJ mol^{-1}) of the complexes, at 25°C

Metal ion	log K_1	log K_2	log β_2	$-\Delta G_1$	$-\Delta G_2$	$-\Delta G$
Fe(II)	4.14	4.35	8.49	23.61	24.81	48.42
Co(II)	4.18	4.40	8.58	23.84	25.09	48.93
Ni(II)	4.59	4.49	9.08	26.18	25.61	51.79
Cu(II)	5.16	5.08	10.24	29.43	28.97	58.22
Zn(II)	4.07	4.35	8.42	23.21	24.81	48.02
Cd(II)	4.01	4.33	8.34	22.87	24.69	47.56

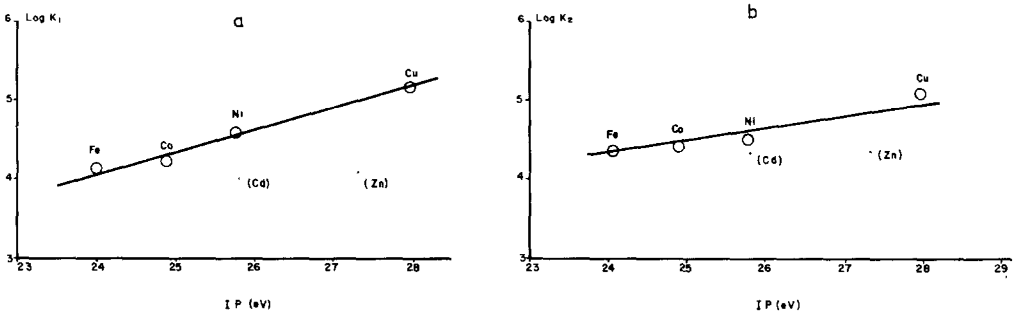


Fig. 2. Plots of (a) log K_1 and (b) log K_2 vs. IP.

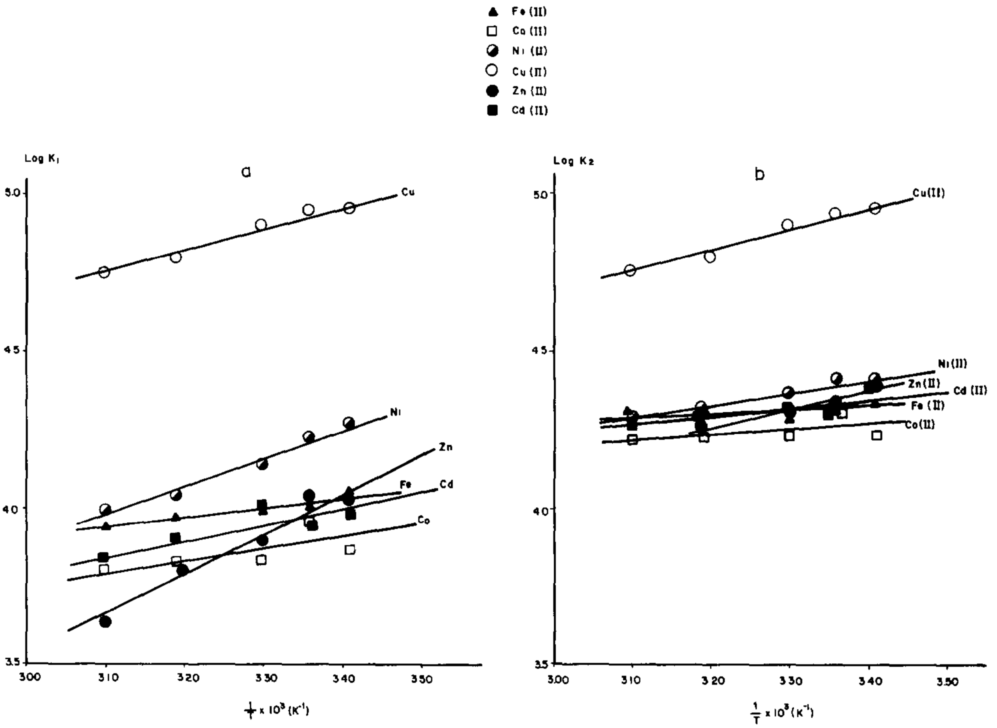


Fig. 3. Plots of (a) log K_1 and (b) log K_2 vs. $1/T$ for the complexes at 0.1 M ionic strength.

TABLE 5

Enthalpy (kJ mol^{-1}) and entropy changes (in J mol^{-1} K^{-1}) in the formation of 1/1 and 1/2 complexes (0.1 M ionic strength of KNO_3)

Metal ion	$-\Delta H_1$	$-\Delta H_2$	$-\Delta H$	ΔS_1	ΔS_2	ΔS
Fe(II)	5.20	1.24	6.44	59.33	78.27	137.60
Co(II)	6.99	3.68	10.67	50.91	69.28	120.19
Ni(II)	17.57	6.73	24.30	21.62	61.24	82.86
Cu(II)	13.57	12.72	26.29	48.80	51.67	100.47
Zn(II)	24.79	11.28	36.07	−6.70	45.36	38.66
Cd(II)	8.58	4.31	12.89	47.27	68.32	115.59

the complexation processes were calculated on the basis of the relation $\log K_i = -\Delta H_i/2.303RT + \Delta S_i/2.303R$; the data obtained are summarized in Table 5. This table shows that all the processes are exothermic; thus, enthalpy values are favourable for the formation processes. In addition to that, ΔH_1 are considerably higher than ΔH_2.

On the other hand, ΔS_1 and ΔS_2 values are all positive (except ΔS_1 of the LH/Zn(II) system) and, consequently, also favourable for the complexation processes. Nevertheless, on comparing ΔS_1 with ΔS_2 values it can be seen that ΔS_2 are considerably higher than ΔS_1 in all the systems in which the formation constants K_2 are higher than those for K_1 (Fe(II), Co(II), Zn(II) and Cd(II)). Therefore, assuming that ΔH values are related to the strength of the metal–ligand bond [21], the above data may indicate that the entropy is responsible for the minor stability of the 1/1 complexes, in the four systems discussed.

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