Thermochimica Acta, 89 (1985) 141–149
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

INFLUENCE OF IONIC STRENGTH ON STABILITY CONSTANTS OF Ag(I), Zn(II), Cd(II) AND Hg(II) COMPLEXES WITH SOME 4-AMINO-5-NITROSO-PYRIMIDINE DERIVATIVES

M.N. MORENO-CARRETERO

Department of Inorganic Chemistry, University College, 23071-Jaen (Spain)

J.M. SALAS-PEREGRIN *

Department of Inorganic Chemistry, Faculty of Sciences, University of Granada, 18071-Granada (Spain)

(Received 7 January 1985)

ABSTRACT

The stability constants, K_1, of the complexes formed by 4-amino-2,6-dioxo-3-methyl-5-nitroso-1,2,3,6-tetrahydro-pyrimidine (LH), 4-amino-1,3-dimethyl-2,6-dioxo-5-nitroso-1,2,3,6-tetrahydro-pyrimidine (RH) and 4-amino-1,6-dihydro-1-methyl-2-methoxy-5-nitroso-6-oxo-pyrimidine (JH) with Ag(I), Zn(II), Cd(II) and Hg(II) ions, in aqueous media at different ionic strengths and 25°C, have been calculated by Bjerrum's method.

From the data obtained, thermodynamic stability constants have been calculated, in each case, using the Debye–Hückel limit law and adjusting log K_1 vs. $\sqrt{I}$ values at a parabolic equation by least-squares methods. The log K_1^0 values, calculated by both methods, are in good agreement.

INTRODUCTION

Recently, the importance of metal ions to the vital functions in living organisms, and, hence, their health and well-being, has become increasingly apparent [1–5]. For this reason, and, especially, because of the chemiotherapeutic effects that some of these complexes have shown [6–12], the study of interactions between metal ions and components of nucleic acids (pyrimidine and purine derivatives and their nucleosides and nucleotides) has been tackled by numerous investigators, yielding, as a consequence, a great number of publications in recent years [13,14].

As a continuation of our research about the stability of metal–pyrimidine complexes in aqueous solutions [15], we report in this paper the influence of ionic strength of the medium on the stability constants of Ag(I), Zn(II),

---

* To whom all correspondence should be addressed.

Cd(II) and Hg(II) complexes with 4-amino-2,6-dioxo-3-methyl-5-nitroso-1,2,3,6,-tetrahydro-pyrimidine (LH), 4-amino-1,3-dimethyl-2,6-dioxo-5-nitroso-1,2,3,6-tetrahydro-pyrimidine (RH) and 4-amino-1,6-dihydro-1-methyl-2-methoxy-5-nitroso-6-oxo-pyrimidine (JH).

EXPERIMENTAL

All the chemicals used in this work were analytical reagent grade. The solutions were prepared in double-distilled, carbon dioxide-free water. Solutions of different ligands (4×10^{-4} M) were prepared by direct weighing from pure samples, synthesized by us following previously reported methods [16]. Solutions of silver(I), zinc(II) and cadmium(II) nitrates, as well as mercury(II) chloride were prepared and standardised. A suitable volume of each solution was diluted to 5×10^{-3} M.

In the case of Ag(I), Zn(II) and Cd(II) complexes, a standardised solution of KNO_3 (2.5 M) was used to maintain the required ionic strength, while for Hg(II) complexes, a KCl solution, with the same characteristics, was employed. A solution of carbonate-free potassium hydroxide (0.01 M) was prepared and standardised.

Apparatus

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

Bjerrum's method [17] was employed in this study. In each case, a solution (initial volume 25 ml), in which $[M^{n+}] = [\text{ligand}] = 2 \times 10^{-4}$ M, was titrated against a standard alkali (0.01 M KOH) after adjusting its ionic strength and temperature (25°C in all cases) in a thermostatted bath.

According to the employed method [17], the ratio of metal to ligand concentration was kept at 1 : 1 in order to calculate the corresponding K_1 values.

RESULTS AND DISCUSSION

The values of $\bar{n}$ and pA (A = L, R, J) were calculated from the pH titration curves following Bjerrum's method [17]. The previously reported [18–20] values of the ionization constants for the ligands were used here. The formation curves between $\bar{n}$ and pA were plotted and, by interpolation at $\bar{n} = 0.5$, the corresponding log K_1 values were obtained for each metal–ligand complex. These values, at 25°C and different ionic strengths, are given in Table 1.

TABLE 1

Stability constants of complexes at 25°C and different ionic strengths

I (mol l^{-1})	M^{n+}/LH				M^{n+}/RH				M^{n+}/JH			
	Ag(I)	Zn(II)	Cd(II)	Hg(II)	Ag(I)	Zn(II)	Cd(II)	Hg(II)	Ag(I)	Zn(II)	Cd(II)	Hg(II)
0.01	6.09	4.92	4.15	5.44	4.13	4.54	4.15	4.89	4.69	5.82	4.49	6.40
0.02	6.05	4.75	4.13	5.20	4.12	4.50	4.14	4.75	4.66	5.76	4.46	6.25
0.04	6.00	4.62	4.13	4.92	4.11	4.44	4.17	4.50	4.60	5.65	4.42	6.01
0.06	5.97	4.50	4.13	4.65	4.10	4.40	4.16	4.38	4.55	5.60	4.39	5.86
0.10	5.91	4.48	4.17	4.45	4.08	4.39	4.13	4.32	4.47	5.59	4.35	5.56
0.20	5.87	4.49	4.14	4.33	4.09	4.39	4.15	4.26	4.45	5.55	4.33	5.10
0.30	5.82	4.51	4.17	4.28	4.10	4.40	4.12	4.20	4.42	5.51	4.32	4.76
0.40	5.79	4.48	4.17	4.25	4.10	4.39	4.13	4.15	4.40	5.50	4.31	4.50
0.50	5.74	4.50	4.14	4.22	4.09	4.39	4.11	4.08	4.40	5.48	4.32	4.25

In this table, it can be observed that the stability constants of complexes with JH are similar to those found for analogous complexes with 4-amino-1,6-dihydro-1-methyl-2-methylthio-5-nitroso-6-oxo-pyrimidine [15], uracil, thymine and cytosine [21–24] and some violuric acids [25–27], while the corresponding values for RH and LH complexes are, in general, lower.

Except in the cases of Cd(II)/LH and Cd(II)/RH complexes, in which the stability constants are not affected, the stability of complexes decreases with increasing ionic strength of the medium. This fact is in agreement with the observations related by Debye [28] and can be justified using the extended Debye–Hückel equation concept, which implies that the mean distance of closest approach for the ligands to the metal ion is larger in salt solutions, since the negatively charged atmosphere around the cation is denser in solutions of greater ionic strength. This prevents the close approach of ligands to the metal ion and, consequently, hampers complexation processes.

In order to obtain the corresponding thermodynamic stability constants, log K_1^0, we have plotted, according to Debye–Hückel's limit law [29], log K_1 vs. $\sqrt{I}$ (Fig. 1). From these curves, and by extrapolation to zero ionic strength of a straight stretch of them, the values of thermodynamic stability constants can be obtained. These data are listed in Table 2, which includes the corresponding values of free energy (ΔG) for complexation processes, and the range of linearity of the log K_1 vs. $\sqrt{I}$ plot.

Likewise, the values of log K_1 fit the simple empirical equation

$$\log K_1 = a - b\sqrt{I} + cI \tag{1}$$

quite closely over the entire range of ionic strength employed ($0 < I < 0.5$). The adjustment of experimental data in each case to this parabolic relation, by the least-squares method, has allowed values to be obtained for a, b and c coefficients that are 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 equation obtained. This value can be interpreted as a measurement of the accuracy of each fit.

Returning to eqn. (1), it can easily be seen that the parameter a has to coincide, theoretically, with the thermodynamic stability constant value. This can be confirmed by a comparison of a values (Table 3) with log K_1^0 values (Table 2), from which a good agreement for each metal/ligand system can be observed.

On the other hand, considering eqn. (1) in the form $a - \log K_1 = b\sqrt{I} - cI$, it is clear that the difference between thermodynamic and apparent stability constant values is the sum of terms $\sqrt{I}$ and I. According to the theory of electrolytic solutions [30], the $b\sqrt{I}$ term accounts for ion–ion interactions, while the cI term accounts for disturbances in the ion–solvent interactions. Therefore, a consideration of the constants b and c (Table 3) should yield some information about these interactions in these systems. At low ionic

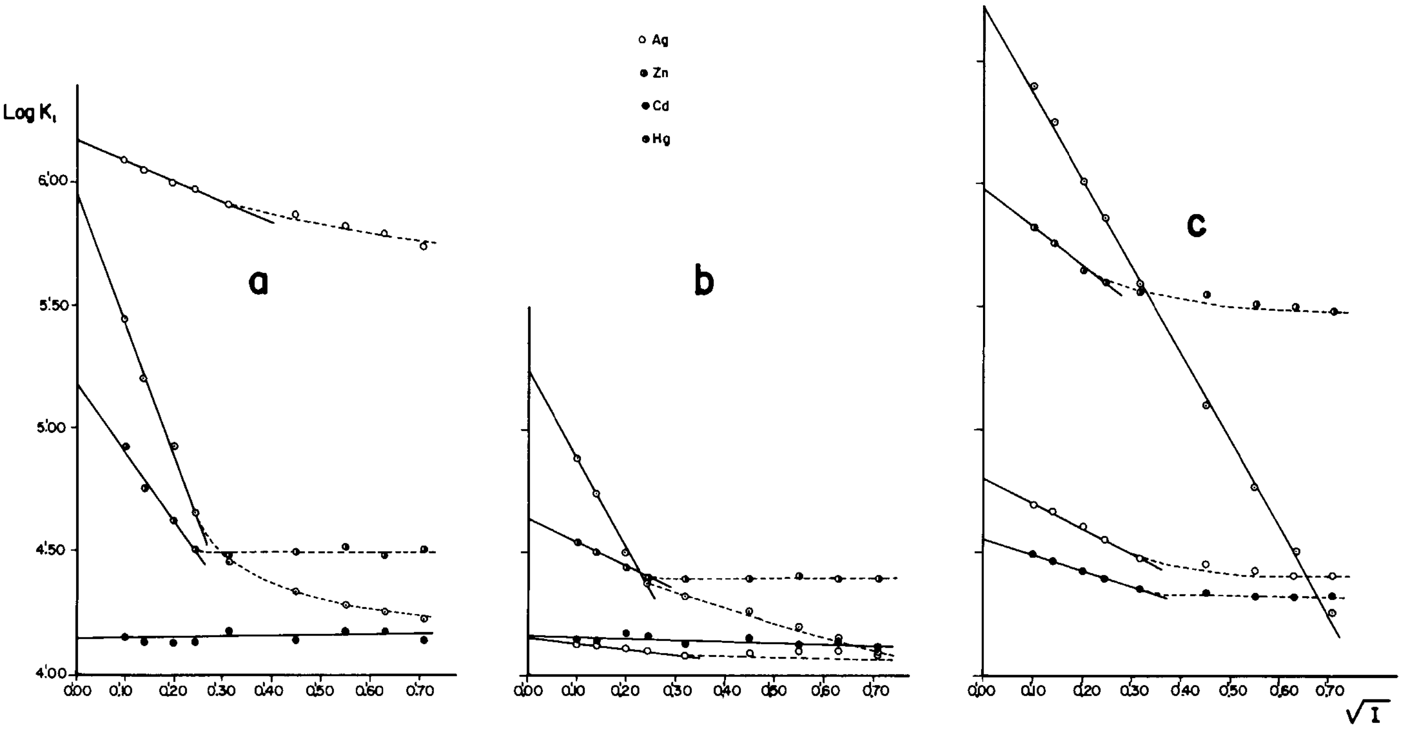

Fig. 1. Plot of log K_1 versus $\sqrt{I}$. (a) M^{n+}/LH, (b) M^{n+}/RH and (c) M^{n+}/JH systems.

TABLE 2

Thermodynamic stability constants of complexes at 25°C calculated by extrapolation to zero ionic strength, using the relation $\log K_1 = \log K_1^0 - a\sqrt{I}$

System	M^{n+}/LH				M^{n+}/RH				M^{n+}/JH			
	Ag(I)	Zn(II)	Cd(II)	Hg(II)	Ag(I)	Zn(II)	Cd(II)	Hg(II)	Ag(I)	Zn(II)	Cd(II)	Hg(II)
Log K_1^0	6.17	5.18	4.14	5.97	4.15	4.64	4.16	5.25	4.80	5.98	4.55	6.73
$-\Delta G$ (kJ mol^{-1})	35.2	29.5	23.6	34.0	23.7	26.5	23.7	29.9	27.4	34.1	25.9	38.4
R [a]	< 0.10	< 0.06	[b]	< 0.06	< 0.10	< 0.06	[b]	< 0.06	< 0.10	< 0.06	< 0.10	[b]

[a] R = interval of ionic strength values for which the relation between log K_1 and $\sqrt{I}$ is linear.

[b] Log K_1 vs. $\sqrt{I}$ linear over the entire range of ionic strength employed.

TABLE 3

Adjustment of experimental values of log K_1 vs. $\sqrt{I}$ to empirical relation (1), by means of the least-squares method

System	M^{n+}/LH				M^{n+}/RH				M^{n+}/JH			
	Ag(I)	Zn(II)	Cd(II)	Hg(II)	Ag(I)	Zn(II)	Cd(II)	Hg(II)	Ag(I)	Zn(II)	Cd(II)	Hg(II)
a	6.16	5.08	4.12	5.95	4.15	4.60	4.15	5.12	4.81	5.92	4.57	6.82
b	0.86	2.64	−0.12	6.22	0.25	0.93	−0.05	3.29	1.33	1.43	0.91	4.19
c	0.41	2.68	−0.11	5.50	0.26	0.93	−0.14	2.71	1.06	1.18	0.79	0.80
S_{yx} [a]	0.01	0.06	0.01	0.07	0.01	0.03	0.01	0.06	0.02	0.03	0.01	0.01

[a] S_{yx} = standard deviation of experimental values of log K_1 with respect to those calculated by the relation obtained.

strength, as the solute ions become separated, the solvent shell of each ion is freed of disturbances and the cI term is negligible. Under these conditions, log K_1 is a linear function of $\sqrt{I}$. On the contrary, at high ionic strength, the term due to ion–solvent interactions acquires more importance with respect to the $b\sqrt{I}$ term becoming, in most of cases, comparable with it. Under these conditions, the values of stability constants are practically unaffected by the increase in ionic strength of the medium, since the difference between both terms is approximately constant.

Finally, the relationship between the values of the thermodynamic stability constants (log K_1^0) of Zn(II), Cd(II) and Hg(II) complexes and the ionization potential (IP) of the corresponding metal ion has been studied. Several authors (ref. 31 and references therein) have pointed out that there is a linear relationship between the ionization potential for a series of metals and the stability of the complexes formed by their corresponding ions with a given ligand. This correlation can be represented by the following equation

$$\log K = p(\mathrm{IP} - q) \qquad (2)$$

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). In order that the values of p and q obtained for each ligand can be compared with those found in the literature [31] for other ligands, the values of K_1^0 (given in l mol^{-1} in Table 2) 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}.

The values of p and q for each ligand at 25°C and in aqueous medium are given in Table 4.

A comparison of these values with those reported in ref. 31 does not permit any conclusion to be made about the type of metal–ligand bond that takes place in these systems, since q values are intermediates between those corresponding to ligands of type I (covalent character of the bond) and type II (coulomb interactions), while p values are in agreement with those corresponding to some ligands containing one functional charged group and other functional uncharged groups, such as 2-amino-phenolato [32], 3-formyl-4-hydroxy-benzenesulphonate [33] and 2-formyl-phenolato [34], when

TABLE 4

Values of p and q for the ligands

	LH	RH	JH
p	1.01	0.59	1.21
q	11.02	6.97	11.62
r [a]	1.000	0.987	0.996

[a] r = correlation coefficient of regression straight line $\log K = p(\mathrm{IP} - q)$.

they act as type I ligands. These are similar to LH, RH and JH ligands if we suppose that in an aqueous solution they are bound to the corresponding metal ion in 5-nitroso-6-oxide form. The anomalous values of q may be explained by steric effects that can be due to a more complicated structure seen in our ligands when compared with those reported in ref. 31.

REFERENCES

1 H.H. Natagani and W.J. Brill, Biochim. Biophys. Acta, 362 (1974) 160.
2 H. Dalton and L.E. Mortenson, Bacteriol. Rev., 36 (1972) 231.
3 E.J. Underwood, Trace Elements in Human and Animal Nutrition, Academic Press, New York, 1971.
4 G.L. Eichhorn, Inorganic Biochemistry, Vol. 2, Elsevier, Amsterdam, 1973.
5 T.G. Spiro, Nucleic Acid–Metal Ion Interactions, Wiley, New York, 1980.
6 A. Goodman, L.S. Goodman and A. Gilman, The Pharmacological Basis of Therapeutics, Macmillan, New York, 1980.
7 B. Rosenberg, Cancer Chemother. Rep., 59 (1975) 589.
8 B. Lippert, J. Clin. Hematol. Oncol., 7 (1977) 26.
9 T.A. Connors, M. Jones, W.C. Ross, P.D. Braddock, A.R. Kokhaz and M.L. Tobe, Chem. Biol. Interact., 5 (1972) 415.
10 R.J. Speer, H. Ridgway, L. Hall, D.P. Stewart, K.E. Howe, D.Z. Lieberman, A.D. Newman and J.M. Hill, Cancer Chemother. Rep., 59 (1975) 629.
11 G.R. Gale, Handb. Exp. Pharmakol., 38 (1975) 829.
12 M. Rozencweig, D.D. von Hoff, M. Slavik and F.H. Muggia, Ann. Intern. Med., 86 (1977) 803.
13 D.J. Hodgson, Progr. Inorg. Chem., 23 (1977) 211.
14 L.G. Marzilli, Progr. Inorg. Chem., 23 (1977) 255.
15 A.M. Martínez-Garzón, R. López-Garzón and M.N. Moreno-Carretero, Thermochim. Acta, 80 (1984) 143.
16 C. Rodriguez-Melgarejo, Thesis, University of Granada, 1979.
17 J. Bjerrum, Metal Ammine Formation in Aqueous Solution, Haase, Copenhagen, 1941.
18 J.D. López-González, C. Valenzuela-Calahorro, J.M. Salas-Peregrin and J.S. García-Mino, An. Quim., 74B (1980) 256.
19 C. Valenzuela-Calahorro, J.D. López-González and R. Galisteo-Tirado, An. Quim., 73 (1977) 1124.
20 C. Valenzuela-Calahorro, J.D. López-González and J.M. Salas-Peregrin, An. Quim., 76B (1980) 197.
21 M.M.T. Khan and M.S. Jyoti, J. Inorg. Nucl. Chem., 40 (1978) 1731.
22 R.C. Srivastava and M.N. Srivastava, J. Inorg. Nucl. Chem., 40 (1978) 1439.
23 A. Reinert, Abh. Dtsch. Akad. Wiss. Berlin, Kl. Med., 6 (1964) 373.
24 M.M.T. Khan and C.R. Krishnamoorthy, J. Inorg. Nucl. Chem., 36 (1974) 711.
25 P. Mathur, D.P. Goel and R.P. Singh, J. Indian Chem. Soc., 55 (1978) 879.
26 P. Mathur, D.P. Goel and R.P. Singh, Z. Naturforsch, Teil B, 31 (1976) 1096.
27 P. Mathur, D.P. Goel and R.P. Singh, Indian J. Chem., 16A (1978) 890.
28 P. Debye, Trans. Electrochem. Soc., 82 (1942) 7.
29 M. Diaz-Peña and A. Roig-Muntaner, Química Física, Vol. II, Alhambra, Madrid, 1978.
30 R.W. Gurney, Ionic Processes in Solution, Dover Publications, New York, 1962.
31 C.L. Van Panthaleon, Recl. Trav. Chim., Pays-Bas, 72 (1953) 50.
32 R.G. Charles and H. Freiser, J. Am. Chem. Soc., 74 (1952) 1385.
33 M. Calvin and N.C. Melchior, J. Am. Chem. Soc., 70 (1948) 3270.
34 L.E. Maley and D.P. Mellor, Aust. J. Sci. Res., Ser. A, 2 (1949) 92.