Inorganica Chimica Acta, 56 (1981) L75–L76

Stereoselectivity in Mixed Zinc(II)–Histidine–Threonine Complex

ARTHUR GERGELY

Institute of Inorganic and Analytical Chemistry, Lajos Kossuth University, H-4010 Debrecen, Hungary

Received June 25, 1981

Introduction

The interactions of transition metals with histidine were previously reviewed by Sundberg and Martin [1]. Stereoselectivity was established for the bis zinc(II) complex, in spite of its approximately tetrahedral structure. In solution mixed D, L complex formation is favoured [2], and thus a weak bond exists between the carboxylate group and the metal. Pettit and Hefford [3] recently surveyed stereoselectivity in the metal complexes of amino acids and dipeptides. A similar effect was found in zinc(II) complexes of some substituted histidines and in their ternary complexes formed with histidine [4, 5].

Though mixed zinc(II) histidine complexes are of appreciable significance in biological systems [6], only lately has attention been paid to their study [7, 9]. In the case of the zinc(II)–histidine–glycine system a definite stabilization was found. This was also proved [10] for the zinc(II)–histidine–alanine and zinc(II)–histidine–phenylalanine systems.

Alemdaroglu and Berthon [11] found a value of −0.22 for the $\Delta\log\beta_{111}$ of the histidine–threoninate mixed complex, *i.e.* a relatively high destabilization takes place. This phenomenon was attributed to the interaction of the carboxy group of histidine with the hydroxy group of threonine. The hydroxy group might play a role in complex formation [12], but its effect in the mixed complexes could additionally depend on the optical configuration of the ligands. To verify this equilibrium measurements were carried out on zinc(II)–D-histidine interactions with the optically active ligands alanine, serine and threonine.

Experimental

L-histidine (his), L-serine (ser) and L/D-α-alanine (ala) were purchased from Reanal; L/D-threonine (thr) was a Merck product. The amino acids were purified by recrystallization from aqueous ethanol. A $ZnCl_2$ stock solution was prepared.

Though the stability constants of the appropriate binary complexes are known [7, 8, 12], they were re-determined during the present work. The metal concentration was in each sample 2.10^{-3} mol dm^{-3}, while those of the ligands depended on the metal to ligand ratios. To obtain the stability constants of the binary complexes, samples with 1:1, 1:2 and 1:4 metal to ligand ratios were titrated with 0.2 mol dm^{-3} KOH in the range of pH 6–9. In the case of ternary complexes titrations were performed at metal to ligand *A* and *B* ratios of 1:1:1, 1:2:1, 1:1:2 and 1:2:2, in the range pH 5–9 or until precipitation.

A Radiometer pHM 64 pH-meter with a GK-2301 combined electrode was used.

Determination of the concentrations of the solutions, and also the pH-metric examinations and their evaluation, were performed as described previously [13, 14].

Results and Discussion

The stability constants relating to the zinc(II)–L/D-ala, zinc(II)–L-ser and zinc(II)–L/D-thr systems are listed in Table I.

The values determined in this work for the complexes of ala, ser and thr, taking into account the difference in the ionic strengths, are in good agreement with those found earlier [8]. In addition there was no difference between the titration data for the zinc(II)–L-ala and zinc(II)–D-ala systems. Nevertheless in the case of the zinc(II)–L-thr and zinc(II)–D-thr systems there was a small but definite difference between the respective results. Hence, the stability constants were calculated separately for the L and D forms and, in addition, measements were performed with the mixed zinc(II) (+ thr) (− thr) system too.

TABLE I. Stability Constants of Some Zinc(II)–L/D-amino Acid Complexes. t = 25 °C; I = 0.2 mol/dm^3 (KCl).

	$\log\beta$			
	ZnA	$ZnAH_{-1}$	ZnA_2	ZnA_2H_{-1}
L/D-alanine	4.56 ± 0.03	−3.60 ± 0.08	8.51 ± 0.03	−0.2 ± 0.2
L-serine	4.45 ± 0.03	−3.73 ± 0.06	8.16 ± 0.05	−2.4 ± 0.4
L-threonine	4.53 ± 0.02	−4.09 ± 0.09	8.38 ± 0.02	−1.5 ± 0.1
D-threonine	4.54 ± 0.02	−4.0 ± 0.09	8.40 ± 0.03	−1.5 ± 0.1
L/D-threonine	4.54 ± 0.01	−4.2 ± 0.1	8.45 ± 0.02	−1.4 ± 0.1

The equilibrium data obtained are given in Table I: it can be seen that the logβ value for the zinc(II) (+ thr) (– thr) optically mixed complex does differ, though to only a small extent, from those for the complexes formed with the optically pure ligands. Thus, the interaction between the thr hydroxy group and the metal is probably very weak, and therefore the stereoselective effect in the zinc(II)–thr parent complex, manifested in these slight differences, can be neither definitely excluded nor supported.

On the basis of the data obtained for the zinc(II)–thr systems, experiments were carried out using serine only, with the L form of the ligand. The stability constant for the zinc(II)$(his)_2$ complex was determined earlier [9]; its logβ_{120} value is 11.84.

TABLE II. Stability Data on Some Zinc(II)–L-histidine–L/D-amino Acid Mixed Ligand Complexes. t = 25 °C; I = 0.2 mol/dm^3 (KCl).

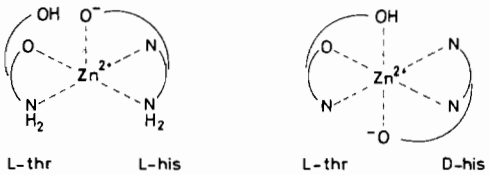
	log β_{111}	Δlogβ_{111}
Zn–L-his–L-ser	10.14 ± 0.05	–0.16
Zn–L-his–L-thr	10.10 ± 0.06	–0.31
Zn–L-his–D-thr	10.48 ± 0.03	+0.06
Zn–L-his–gly	10.89 ± 0.05	+0.16
Zn–L-his–L-ala	10.58 ± 0.07	+0.10
Zn–L-his–D-ala	10.58 ± 0.07	+0.10

Equilibrium data relating to the mixed zinc(II)-histidine-amino acid complexes are listed in Table II. From the data in Table II the following conclusions can be drawn:

(i) There is no difference in the stabilities of the zinc(II)–L-his–L-ala and zinc(II)–L-his–D-ala complexes, and their Δlogβ_{111} values are similar to those found earlier [9] for the zinc(II)–L-his–glycine system. As a consequence, the optical activity of the ala ligand has no influence on the mixed ligand formation with zinc(II)–his.

(ii) The situation is different with the mixed complex formation of the thr ligand. As can be seen in Table II, a high de-stabilization was found for zinc(II)–L-his–L-thr, a result which resembles that obtained by Alemdaroglu and Berthon [11] and which is in accordance with the value for the zinc(II)–L-his–L-ser mixed complex. On the other hand, stabilization exists in the mixed zinc(II)–L-his–D-thr complex which, in addition, contains optically mixed L/D amino acids. This finding is in good agreement with that observed by Morris and Martin [2] for the zinc(II)–his parent complex which was explained in terms of the stereoselective effect.

(iii) The stereoselective effect observed in the mixed complexes containing an alcoholic hydroxy group in the side-chain of the amino acids can be interpreted in the same way as the zinc(II)–his parent complex. Zinc(II)–his has a distorted octahedral structure and a cis arrangement of the donor groups around the metal. This structure also holds in the mixed zinc(II)–his–thr complex.



In the structure of the mixed zinc(II)–L-his–L-thr complex, bonding of the carboxylate group of the his is hindered. This hindrance can be attributed either to competition between the carboxylate and the alcoholic hydroxy group for bonding to the metal, or to hydrogen bonding between the two groups. The latter assumption seems to be less likely than does the first, for in the zinc(II)–thr parent complex the possibility of a stereoselective effect cannot be excluded.

The *cis* arrangement of the donor groups around the zinc(II) on the other hand favours mixed complex formation in the zinc(II)–L-his–D-thr system. In this case therefore its concentration maximum is higher than in the statistical case.

Acknowledgements

The author is indebted to Dr. Tamás Kiss for his valuable contribution to this work.

References

1 R. J. Sundberg and R. B. Martin, *Chem. Rev., 74,* 471 (1974).
2 P. J. Morris and R. B. Martin, *J. Inorg. Nucl. Chem., 32,* 2891 (1970).
3 L. D. Pettit and R. J. Hefford, Metal Ions in Biological Systems, Vol. 9 (H. Sigel, ed.), Marcel Dekker, New York, 1979.
4 G. Brookes and L. D. Pettit, *J. Chem. Soc. Dalton,* 1224 (1976).
5 J. H. Ritsma, *J. Inorg. Nucl. Chem., 38,* 907 (1976).
6 G. Berthon, C. Matuchansky and P. May, *J. Inorg. Biochem., 13,* 63 (1980).
7 P. G. Daniele and G. Ostacoli, *J. Inorg. Nucl. Chem., 40,* 1273 (1978).
8 D. D. Perrin, Stability Constants of Metal-Ion Complexes: Part B, Organic Ligands, Pergamon Press, Oxford, 1979.
9 I. Sóvágó, T. Kiss and A. Gergely, *J. Chem. Soc. Dalton,* 964 (1978).
10 G. S. Malik, S. P. Singh and J. P. Tandon, *J. prakt. Chem., 320,* 324 (1978).
11 T. Alemdaroglu and G. Berthon, *Inorg. Chim. Acta (B)* (in press).
12 A. Gergely, J. Mojzes and Zs. Kassai-Bazsa, *J. Inorg. Nucl. Chem., 34,* 1277 (1972).
13 A. Gergely, I. Nagypál and E. Farkas, *Acta Chim. Acad. Sci. Hung., 82,* 43 (1974).
14 I. Nagypál, *Acta Chim. Acad. Sci. Hung., 82,* 29 (1974).