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Complex Formation Studies on Copper(II) and Zinc(II) with Asparagine and Aspartic Acid in Aqueous Solution

Short Communication

Lechosław Łomozik*, **Anna Wojciechowska**, and **Mariusz Jaskólski**

Faculty of Chemistry, Adam Mickiewicz University, PL-60-780 Poznań, Poland

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The complex equilibria of the systems copper—aspartic acid, zinc—aspartic acid, copper—asparagine, and zinc—asparagine have been studied by computer analysis of potentiometric data.

[Keywords: Asparagine; Aspartic Acid; Complexes; Copper(II); Formation constants; Zinc(II)]

Untersuchungen zur Komplexbildung von Kupfer(II) und Zink(II) mit Asparagin und Asparaginsäure in wäßrigen Lösungen (Kurze Mitteilung)

Anhand einer Computer-Analyse von potentiometrischen Daten wurden die Systeme Kupfer—Asparaginsäure, Zink—Asparaginsäure, Kupfer—Asparagin und Zink—Asparagin untersucht.

Studies of the reactions of metal ions with amino acids and peptides are an important field of coordination chemistry due to the role played by metals in biological systems.

Containing one amino and two carboxyl groups, aspartic acid can act as a tridentate ligand. Its amide derivative, asparagine, usually reacts with metals as a bidentate ligand. A number of papers have been published so far with the results of studies on the complexes formed by zinc and copper with asparagine and aspartic acid[1–6].

This paper presents our results of the equilibrium studies of copper and zinc complexes with asparagine and aspartic acid.

The program SCOGS[7] was used for the least-squares refinement of the formation constants using potentiometric titration data as input. The equilibrium concentrations of all species in the investigated systems were computed using HALTAFALL[8]. The measurements were carried out at 21 ± 1 °C in an inert atmosphere of argon. The ionic strength was $\mu = 0.1$ ($NaClO_4$).

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The titration curve for aspartic acid (*AspA*) has an equivalence point at $a = 2$ corresponding to neutralization of the two carboxyl groups. Analogous equivalence point for asparagine (*Asn*) appears at $a = 1$ and corresponds to neutralization of the carboxyl proton of the ligand. Addition of Cu^{2+} or Zn^{2+} results in a decrease of the buffer regions with respect to the free-ligand systems. Copper reacts with both ligands at significantly lower *pH* values and its buffer region lies appreciably below that of Zn^{2+}. In the case of the latter cation it was necessary to use at least five-fold excess of the ligand to avoid precipitation. Composition of each complex-system was determined using SCOGS. In addition to the various criteria for the selection of species proposed so far[9] we used a test consisting in tracing the changes of the amino acid association constants during the refinement of the formation constants.

Table 1. *Overall stability constants of the proton, copper(II) and zinc(II) complexes with aspartic acid and asparagine*

Aspartic acid	logβ	Asparagine	logβ
H_3L^+	15.24 (1)	H_2L^+	10.92 (1)
H_2L	13.50 (1)	HL	8.91 (1)
HL^-	9.76 (1)	ZnL^+	4.52 (9)
ZnL	5.90 (13)	ZnL_2	7.86 (9)
ZnL_2^{2-}	10.17 (14)	CuL^+	7.69 (2)
CuL	9.14 (5)	CuL_2	14.38 (4)
CuL_2^{2-}	16.16 (7)	$CuLOH$	2.33 (7)
$CuHL^+$	12.43 (3)		
$CuLOH^-$	3.54 (20)		

Zinc, under the investigated conditions, forms with both *AspA* and *Asn* only ML and ML_2 complexes. The coordination modes for these two ligands must be quite different, since the corresponding stability constants differ by as much as 1.4 logβ units (ML, Table 1). In both systems, i.e. Zn/*Asn* and Zn/*AspA*, formation of the ML complex starts at $pH = 4.1$.

The systems of copper complexes are far more complicated. For Cu/*AspA* the following complexes have been recognized: ML, ML_2, MHL, and $MLOH$. The Cu/*Asn* system does not contain the protonated MHL species and can be described to consist of ML, ML_2, and $MLOH$. For copper, similarly as it was found for zinc, the ML complex with *AspA* is by 1.5 orders of magnitude more stable than that with *Asn* (Table 1). Formation of the Cu complexes starts at far lower

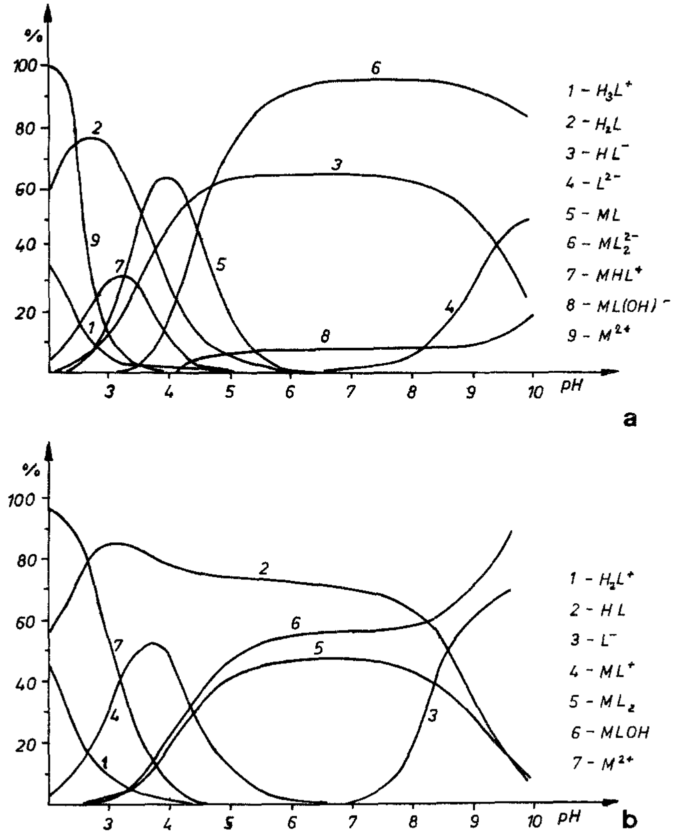

Fig. 1. Distribution diagram of the systems: *a AspA*/Cu, *b Asn*/Cu; percentages of the species refer to total metal except for the metal-free forms which refer to total ligand

pH than in the case of Zn. The CuHL species with *AspA* as the ligand appears at $pH \sim 2$ (Fig. 1). The formation of the protonated complex CuHL (in the Cu/*AspA* system) is the result of a reaction of the H_2L zwitterion with Cu^{2+}:

$$M + H_2L \rightleftharpoons MHL + H$$

The equilibrium constant of this reaction $\left(K_e = \frac{\beta_{MHL}}{\beta_{H_2L}}\right)$ is $\log K_e = -1.07$. The protonation constant of the MHL complex $\left(K^{H}_{MHL} = \frac{\beta_{MHL}}{\beta_{ML}}\right)$ is $\log K^{H}_{MHL} = 3.29$.

Selection of complex forms based on the experimental data shows that $M(\mathrm{OH})_x$ complexes do not exist in the investigated systems. Consequently, the formation of the $ML\mathrm{OH}$ complex observed for both Cu/*AspA* and Cu/*Asn* must start via addition of OH^- to the existing ML complex.

$$ML + \mathrm{OH} \rightleftharpoons ML\mathrm{OH} \tag{1}$$

This assumption is supported by the distribution of various complexes vs. *pH*. $ML\mathrm{OH}$ is formed only when ML is already present in the system. The shapes of curve 8 in Fig. 1 a and curve 6 in Fig. 1 b indicate, however, that the concentration of $ML\mathrm{OH}$ is significantly increased at *pH* ~ 9. At this *pH* the ML complex practically does not exist. The increase of the $ML\mathrm{OH}$ concentration is accompanied by a compatible decrease of the ML_2 concentration (compare curves 6 and 8 in Fig. 1 a and curves 5 and 6 in Fig. 1 b). It can be concluded that OH^- competes with the ligands and that the hydroxy complex in basic solution is formed according to the following scheme:

$$ML_2 + \mathrm{OH} \rightleftharpoons ML\mathrm{OH} + L \tag{2}$$

At the same time, the color of the Cu/*AspA* and Cu/*Asn* systems changes at *pH* ~ 9 from blue to deep violet. The *pH* range of this change corresponds to the above mentioned significant increase of the $ML\mathrm{OH}$ concentration.

A detailed computer analysis of the experimental data excluded all hydroxy complexes but $\mathrm{Cu}L\mathrm{OH}$. We therefore conclude that in acidic conditions a blue $\mathrm{Cu}L\mathrm{OH}$ complex is formed according to eq. (1) whereas under basic conditions reaction (2) leads to a deep violet $\mathrm{Cu}L\mathrm{OH}$ complex characterized by a different structure and a different stability constant.

Further spectroscopic studies, and possibly also X-ray structural investigations, would be necessary to support the above conclusion.

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