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STUDY ON INTERACTIONS OF DIVALENT METAL IONS WITH ASPARTIC ACID IN BINARY COMPLEXES

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ABSTRACT

The acidity constants of aspartic acid (ASP) were determined by potentiometric pH titration. The stability constants of the 1 : 1 complexes formed between M^{2+}: Mn^{2+}, Co^{2+}, Cu^{2+} or Zn^{2+} and Asp^{2-}, were determined by potentiometric pH titration in aqueous solution (I = 0.1 M, $NaNO_3$, 25°C). The order of the stability constants was reported. It is shown that the stability of the binary M (Asp) complexes is determined solely by the basicity of the carboxylate or amin groups. The observed stability order for aspartate follows the Irving-Williams sequence. It is shown that Asp can exert a direct influence on reaction rate through both the kind of metal ions and the kind of donor groups of Asp.

Key words: Aspartic acid, Divalent metal ions, Potentiometric titration, Acidity, Stability constants.

INTRODUCTION

Aspartic acid (L-Aspartic acid) (Fig. 1) and glutamic acid play important roles as general acids in enzyme active centers, as well as in maintaining the solubility and ionic character of proteins. Aspartic acid can help protect the liver from some drug toxicity and the body from radiation. Aspartic acid also can help form the ribonucleotides that assist production of DNA and RNA and aids energy production from carbohydrate metabolism. Aspartic acid may also help improve the function of the immune system, and may play a role in protecting against toxins and neural and brain disorders. Aspartic acid reportedly helps treat chronic fatigue. Aspartic acid can be easily converted to glucose when demand for glucose exceeds supply[1,2].

Aspartic acid is one of the 20 amino acids commonly found in animal proteins. Aspartic acid is the carboxylic acid analog of asparagine. Aspartic acid is alanine with one of the β-hydrogens replaced by a carboxylic acid group. Aspartic acid is a part of organic molecules containing an amino group, which can combine in linear arrays to form proteins in living organisms. Its acidic side chain adds a negative charge and hence a greater degree of water-solubility to proteins in neutral solution and has been shown to be near the active sites of some enzymes. Aspartic acid is a non-essential amino acid having an acidic carboxyl group on its side chain which can serve as both an acceptor and a donor of ammonia. It is converted to l-asparagine by binding with ammonia. It forms carbamyl-l-aspartic acid which roles purine as well as pyrimidine biosynthesis. The peptide RDDANG binds calcium with a significantly greater affinity than does peptide DRNADG. The stronger bonding of calcium to a peptide with Asp residues next to each other has

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analogy with organic diacids that have nearby carboxylic groups and have lower pKa_1's than those with remote functional groups[3,4]. The close proximity of one carboxyl group to another enhances the acidity of the latter. It is of great interest the knowledge of the affinity of aspartic acid for other metal ions and the structure which shows the position of functional groups in M-Asp complexes. This would help us to understand such reation mechanism much better.

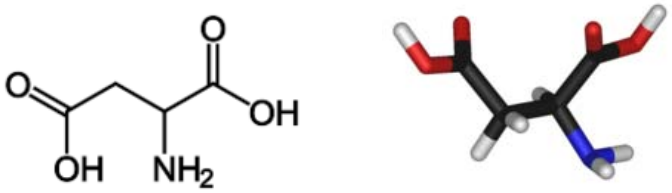

Fig. 1: Chemical structure of L-Aspartic acid

EXPERIMENTAL

Materials

The L-aspartic acid (extra pure) was purchased from Merck, Darmstadt. The nitrate salt of Na^+, Mn^{2+}, Co^{2+}, Cu^{2+} and Zn^{2+} (all pro analysi) were from Merck. All the starting materials were of reagent grade and used without further purification. Potassium hydrogen phthalate and standard solutions of sodium hydroxide (titrasol), nitric acid, EDTA and of the buffer solutions of pH 4.0, 7.0 and 9.0, were from Merck. All solutions were prepared with deionized water. Water was purified by Milil-Q water purification system, deionized and distillated.

pH titrations

Reagents

Carbonate-free sodium hydroxide 0.03 M was prepared and standardized against sodium hydrogen phthalate and a standard solution of nitric acid 0.5 mM. M (II) nitrate solution (0.03 M) was prepared by dissolving the above substance in water and was standardized with standard solution of EDTA 0.1 M (triplex).

Apparatus

All pH titrations was performed using a Metrohm 794 basic automatic titrator (Titrino), coupled with a thermo stating bath Hero at 25°C (± 0.1°C) and a Metrohm combined glass electrode (Ag/AgCl). The pH meter was calibrated with Merck standard buffer solutions (4.0, 7.0 and 9.0).

Procedure

For the determination of acid dissociation constants of the ligand Asp an aqueous solution (0.03 mM) of the protonated ligand was titrated with 0.03 M NaOH at 25°C under nitrogen atmosphere and ionic strength of 0.1 M, $NaNO_3$. For the determination of binary (one ligand and Cu^{2+}) system, the ratios used were 1 : 1, Cu (II) : Ligand and 1 : 1, Cu (II) : Asp, 0.3 mM. This solution was titrated with 0.03 M NaOH under the same conditions mentioned above. Each titration was repeated seven times in order to check the reproducibility of the data.

Calculation

The acid dissociation constants, $K^H_{H_2(Asp)}$ and $K^H_{H(Asp)}$ for H_2(Asp) were calculated by an algebraicmethod. The equilibrium evolved in the formation of 1 : 1 complex of Asp and a divalent metal ion may be expressed as equations 7 and 9.

RESULTS AND DISCUSSION

The potentiometric pH-titrations (25°C, 0.1 M, $NaNO_3$) were carried out to obtain the acidity and stability constants which are summarized in Table 1.

Table 1: Logarithm of the stability constants of binary complexes of M^{2+} at 25°C, 0.1 M, $NaNO_3$*

S. No.	Species	logK	Site
1	H_2(Asp)	3.72 ± 0.03	-CO_2H
2	H(Asp)	9.90 ± 0.03	-NH_3
3	Mn^{2+}	3.91 ± 0.03	-
4	Co^{2+}	6.69 ± 0.06	-
5	Cu^{2+}	8.78 ± 0.02	-
6	Zn^{2+}	5.35 ± 0.06	-

*The given errors are three times the standard error of the mean value or the sum of the probable systematic errors

Acidity constants

Aspartate ion (Asp^{2-}), $^-O_2CCH_2CH(NH_2)CO_2^-$, is a two-basic species and thus it can accept two protons, given H_2 (Asp) for which the following deprotonation equilibriums hold:

$$H_2(Asp) \rightleftharpoons H^+ + H(Asp)^- \quad \ldots(1)$$

$$K^H_{H_2(Asp)} = [H(Asp)^-][H^+]/[H_2(Asp)] \quad \ldots(2)$$

$$H(Asp)^- \rightleftharpoons H^+ + Asp^{2-} \quad \ldots(3)$$

$$K^H_{H(Asp)} = [Asp^{2-}][H^+]/[H(Asp)^-] \quad \ldots(4)$$

The two proton in H_2 (Asp) are certainly bound at the terminal acetate and amino groups, i.e., it is released from $HO_2CCH_2CH(NH_3^+)CO_2^-$ according to equilibrium (1) & (2).

It is also closed to the deprotonation of acetate groups which occurs at the terminal acetate groups of tartaric acid[5,6]. Asp^{2-} can release one more proton from the neutral (NH_2) site of their amin residue, hence, here in addition equilibrium (Eq. 5) should be considered. This takes place above pH ≈ 2.

$$Asp^{2-} \rightleftharpoons H^+ + (Asp\text{-}H)^{3-} \quad \ldots(5)$$

$$K^H_{Asp} = [(Asp\text{-}H)^{3-}][H^+]/[ASP^{2-}] \quad \ldots(6)$$

This reaction is not here further considered.

Stability of binary and ternary complexes

If we abbreviate for simplicity Mn^{2+}, Co^{2+}, Cu^{2+} and Zn^{2+} with M^{2+}, one may write the following two equilibriums Eq. 7 and 9:

$$M^{2+} + H(Asp)^- \rightleftharpoons M(H; Asp)^+ \quad \ldots(7)$$

$$K^{M}_{M(H;Asp)} = [M(H;\ Asp)^{+}]/[M^{2+}]\,[H(Asp)^{-}] \quad \ldots(8)$$

$$M^{2+} + (Asp)^{2-} \rightleftharpoons M(Asp) \quad \ldots(9)$$

$$K^{M}_{M(Asp)} = [M(Asp)]/[M^{2+}]\,[Asp^{2-}] \quad \ldots(10)$$

The experimental data of the potentiometric pH– titrations may be completely by considering the above mentioned equilibriums (Eq. 1-10) if the evaluation is not carried into the pH range where hyrdoxo complex formation occurs.

Potentiometric analyses

The results of all potentiometric pH-titration i.e. acidity and stability constants are summarized in Table 1. The deprotonated amino acid Asp^{2-} can accept in total two protons to give the acid H_2Asp. First one of this two protons of carboxylate residue is released; its pKa is low (≈2). The next proton is the second proton from the carboxylate group. However, Asp^{2-} can release one more proton from neutral - NH_2 site. It is about pH > 12 (eq. 3). The measured acidity constants in this work show good agreement with the same value received by other authors[5,10]. However, the carboxyl group is a far stronger acid than the amino group.

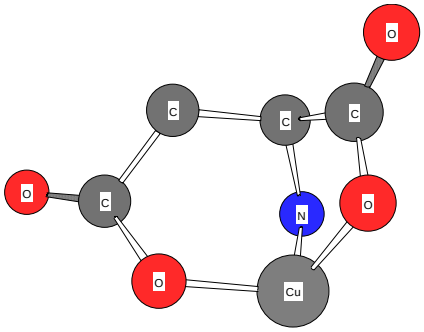

Fig. 2: Schematic structures of the species with interactions according to equilibrium (Eq. 9) for Cu (Asp)

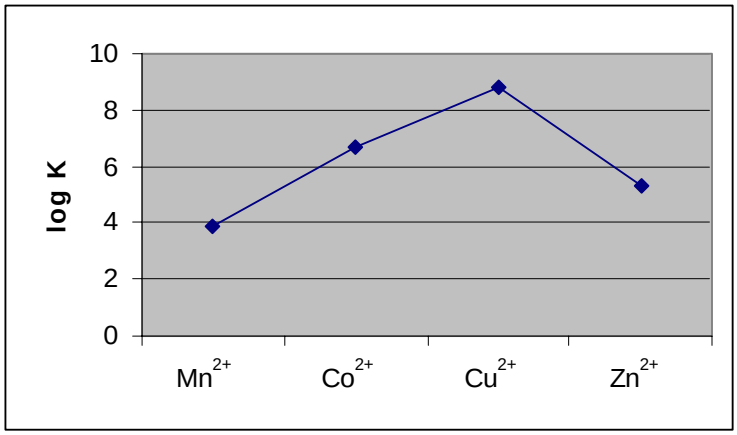

Fig. 3: Irving-Williams sequence-type plot for the 1 : 1 complexes of Mn^{2+} to Zn^{2+} with aspartate (Table 1)

The stability constants of the binary complexes (Fig. 2) were refined separately using the titration data of this system in a 1 : 1, ligand : Cu^{2+} ratio in the same conditions of temperature and ionic strength (according Eq. 7-10). As they were in good agreement with reported value[5,11]. All the stability constants of

Table 1 show the usual trend. The obtained order is $Mn^{2+} < Co^{2+} < Cu^{2+} > Zn^{2+}$. The observed stability order for aspartate follows the Irving-Williams sequence[12] (Fig. 3).

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