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STABILITY CONSTANTS OF COMPLEX FORMATIONS BETWEEN CYCLO(L-HISTIDYL-L-HISTIDYL) AND DIVALENT METAL IONS

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The stability constants of complex formation between cyhis [cyhis= cyclo(L-histidyl-L-histidyl)] as a ligand and some divalent metal ions were determined by Bjerrum's method. The values of $\log K_1$ and $\log K_2$ in this order are: Co, 2.8, 2.3; Ni, 3.8, 2.6; Cu, 6.1, 4.9; Zn, 3.8, 2.9.

In most of the enzymes with metal ions, only the functional groups of the side chains of the peptides coordinate to metal ions. Also, the most important functional groups of their side chains that behave as ligating groups for zinc(II) and copper(II) ions are the imidazole group of the histidine residue. Recently, the structure of $Cu(cyhis)_2(ClO_4)_2 \cdot 4H_2O$ with X-ray structure analysis was obtained by Hori, Kojima, Matsumoto, Ooi, and Kuroya, as a good model of such enzymes as shown in Fig. 1[1] and the structure of the copper complex ion in aqueous solution was already reported elsewhere.[2] Also, the other workers reported the electronic-spectral studies of Cu(II)-imidazole including cyhis as a ligand.[3] It was felt of interest to the present author to measure the stabilities of divalent metal ions with cyhis as a ligand in aqueous solutions. The present letter describes the results of the determination of stability constants of complexes between cyhis and some divalent metal ions by Bjerrum's method.

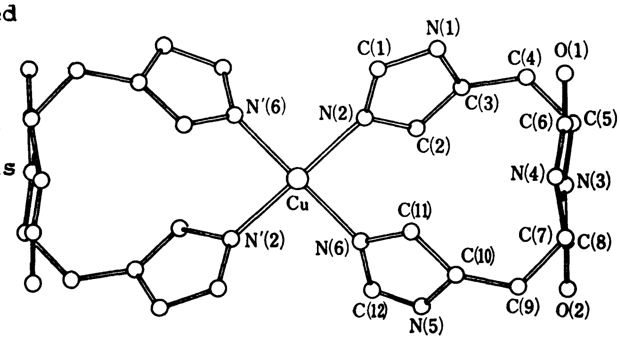
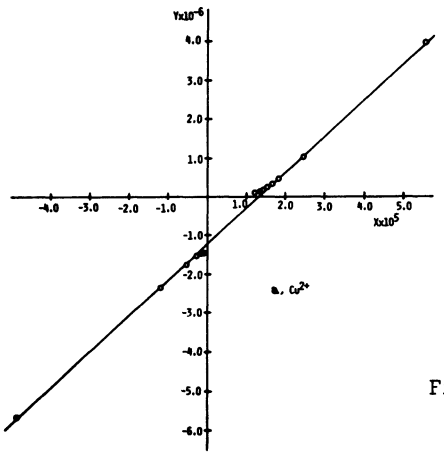


Fig. 1. The structure of $[Cu(cyhis)_2]^{2+}$

In most experments, the solution to be titrated contained 2.19×10^{-4}mol of cyhis, 0.750×10^{-4}mol of $M(NO_3)_2$, and 4.90×10^{-4}mol of HCl in $0.050dm^3$, the ionic strength being adjusted to 0.2 with KNO_3. The M:L ratio in this mixture was ca. 1:3; solutions of other compositions were also examined. The titration curves of the mixtures were obtained under N_2 atomosphere by use of an 0.1022N NaOH solution and an Orion 801A pH meter. The concentration of the free ligand [L] and the average coordination number $\bar{n}$ were caluculated from the titer and the hydrogen ion concentration on the assumption that only 1:1 and 1:2 complexes were formed. The acid dissociation constants K_{a1} and K_{a2} necessary for this calculation were determined also by titration to be $10^{-5.54}$ and $10^{-6.61}$, respectively, at 25°C and $I=0.2(KNO_3)$. The stability constants, $K_1=[ML]/([M][L])$ and $K_2=[ML_2]/([ML][L])$, were then obtained by linear fitting according to the equation, $Y=K_1K_2X-K_1$, where



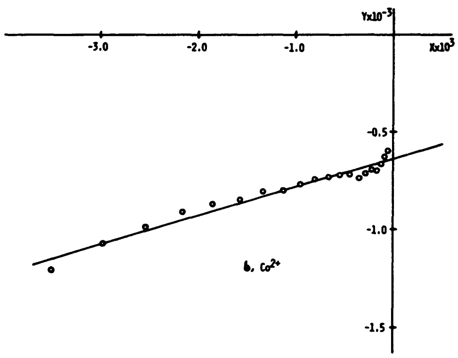


Fig. 2. X-Y plots for determination of stability constants

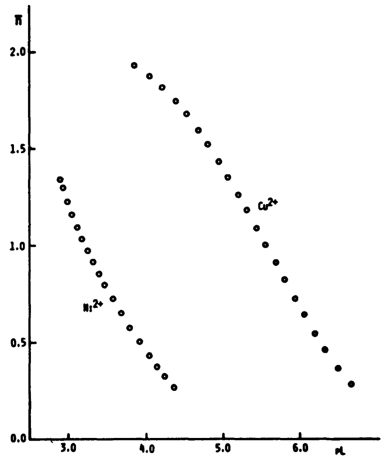


Fig. 3. Formation curves

$X=(2-\bar{n})[L]/(\bar{n}-1)$ and $Y=\bar{n}/\{(\bar{n}-1)[L]\}$. Figs. 2a and 2b illustrate two of such X-Y plots, the former showing the best and the latter the poorest linearity. The values of $\log K_1$ and $\log K_2$ obtained are given in Table 1. They are seen to be in the order of Irving-Williams series. From the usual behavior of Cu^{2+}, it does not seem to be necessary to consider the formation of ML_3 complex for this ion. This can be substantiated by the formation curves, $\bar{n}$ vs. pL shown in Fig. 3. For the other ions it was difficult to conclude from the result of the titration whether ML_3 is formed or not. Attempts to obtain the values of K_3 by successive approximations have not so far been successful, since $\bar{n}$ is usually small as shown for Ni^{2+} in Fig. 3.

Table 1. Stabilities of Complexes between cyhis and divalent metal ions

M	$M_t:L_t$ in solution	$\log K_1$	$\log K_2$
Co	1:2.0	2.8	2.3
	1:3.0	2.8	2.4
Ni	1:1.9	3.80	2.54
	1:2.9	3.79	2.65
	1:3.9	3.75	2.76
Cu	1:2.0	6.09	4.88
	1:2.9	6.20	4.89
Zn	1:2.9	3.8	2.9

The above stability constants seem to have reasonable values in spite of usually unstable 13-membered chelate ring. This is probably because two imidazole groups are held tightly by one diketopiperazine ring so as to facilitate the chelation to the metal ion. However, more experimental results of the similar complexes are necessary for detailed discussions.

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