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Stability Constants of Imidazole- and Alkylimidazole-Copper(II) Complexes

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The stability constants of imidazole (HIm)- and alkylimidazoles–copper(II) acetate complexes were calculated from the potentiometric titration data with the aid of the SUPERQUAD computer program. The stability constants of ionic species of $[CuAL_r]^+$ type (A: CH_3COO, L: HIm **a**, 1-CH_3·Im **b**, 2-CH_3·HIm **c**, 4-CH_3·HIm **d**, 2-C_2H_5·HIm **e**, 2-$(CH_3)_2CH$·HIm **f**, r=1, 2, 3, and 4) detected from the complexes were ascertained to be decreased in the order of **b**(1-substituted)⩾**d**(4-substituted)>**c**(2-substituted) relating to the position of methyl group bonded to the imidazole ring, and **c**(2-CH_3)>**e**(2-C_2H_5)>**f**(2-$(CH_3)_2CH$) relating to the kinds of alkyl group substituted on 2-position, respectively. The stability of these ionic species was discussed from the neutralization effect of the charge and the steric effect of alkyl group or acetate ion. The stability constants of the hydroxo species of $[CuL_2(OH)_2]$ type indicated the extremely small values, and its order did not indicate a similar tendency with those of ionic species of $[CuAL_r]^+$ types. The distribution of these complex species was investigated as a function of pH.

It has been well-known that the metalloproteins, such as plastocyanin,[1)] azurin,[2)] and hemocyanin[3)] formed the active center by the coordination of Cu(II) to imidazole N of histidine residue, play an important roles, biologically. Since we were interested in the situation of coordination of such active center, imidazole–copper(II) acetate complex $[Cu(CH_3COO)_2(HIm)_2]$ (HIm; imidazole), which is similar to the structure of the active center in metalloprotains, was synthesized by the reaction of imidazole and copper(II) acetate monohydrate. It has been already reported by us that this compound is decomposed slowly by refluxing in ethanol.[4)] On the other hand, the stability constants of the ionic species detected from imidazole- and alkylimidazoles–copper(II) acetate complexes ($[Cu(CH_3COO)_2L_r]$, L: HIm **a**, 1-CH_3·Im **b**, 2-CH_3·HIm **c**, 4-CH_3·HIm **d**, 2-C_2H_5·HIm **e**, 2-$(CH_3)_2CH$·HIm **f**, r=1 and 2) were determined by the potentiometric titration method.[5)] The order of stability constants for the ionic species of $[Cu(CH_3COO)L]^+$ was favorably explicable from the relation of the steric hindrance between alkyl groups and acetate ion. However, that for the ionic species of $[Cu(CH_3COO)L_2]^+$ type could not be explained from the influence of steric hindrance. This cause is considered to be due to the calculation which neglected the presence of ionic species other than $[Cu(CH_3COO)L_r]^+$ (r=1 and 2) types.

To solve this question, the acetic acid solutions of imidazole- and alkylimidazoles–copper(II) acetate systems were potentiometrically titrated with sodium hydroxide, and the stability constants from the obtained data were calculated with the aid of the SUPERQUAD computer program.[6)] The stability of ionic species detected was discussed from the influence of the kinds and the substituted position of alkyl group bonded to imidazole ring. Further, the distribution of these ionic species was investigated as the function of pH.

Experimental

Reagents. Imidazole (HIm) **a**, 2-methylimidazole (2-CH_3·HIm) **c**, 4-methylimidazole (4-CH_3·HIm) **d**, 2-ethylimidazole (2-C_2H_5·HIm) **e**, and 2-isopropylimidazole (2-$(CH_3)_2CH$·HIm) **f** of reagent grade were purchased from Kanto Chemical Co., Inc. and Tokyo Kasei, Co., Ltd., and used after recrystallization from benzene, respectively. 1-methylimidazole(1-CH_3·Im) **b** of reagent grade was purchased from Tokyo Kasei Kogyo Co., Ltd., and used after distillation under reduced pressure (51.5 °C/3 mmHg, 1 mmHg=133.322 Pa).

Copper(II) acetate monohydrate of special grade was purchased from Wako Pure Chemical Industries Ltd., and used without further purification. The stock solution of Cu(II) was standardized by the chelatometric titration with 0.01 M solution of EDTA (1 M=1 mol dm^{-3}).

The other reagents of special grade employed were purchased from Wako Pure Chemical Industries Ltd., and used without further recrystallization.

Preparation of Sample Solution. All the sample solution were prepared with distilled water decarbonated.

The sample solutions of 5.017×10^{-3} M acetic acid were prepared to measure the apparent activity coefficient of hydrogen ion (γ_H) and the ionic product of water (k_w).

The sample solution dissolved about 1×10^{-3} M of copper(II) acetate and $(4—12)\times10^{-3}$ M of imidazoles in about 5×10^{-3} M acetic acid were prepared to measure the stability constants of the complex species.

Potentiometric Titration. The sample solution of 50 ml was pipetted in the vessel of 100 ml, and titrated with sodium hydroxide standardized at about 0.1 M under a nitrogen atmosphere. The temperature was maintained at 25±0.1 °C, and the ionic strength was adjusted to 0.1 M with potassium nitrate. The combination glass electrode of Orion 81-20 was calibrated with pH 4.008 and 6.865 buffer solution at 25±0.1 °C. All pH values were estimated with an Orion Research ion Analyser EA-920.

Calculation

The calculation of stability constants were performed by the use of a FACOM M-780/10 computer at Kansai University Information Processing Center.

(1) Apparent Activity Coefficient of Hydrogen Ion and Ionic Product of Water. On the bases of the procedure described in previous paper,[5,7)] γ_H and K_w were calculated from pH value (α_H) obtained by the potentiometric acid-base titration. In this case, the 2.95×10^{-5} was used as the acid dissociation constant of acetic acid at 25 °C.[8)]

$$\gamma_H = \alpha_H/[H] \qquad K_w = \alpha_H[OH] \tag{1}$$

(2) Stability Constants. The overall stability constants (β_{pqrs}) of complex species are represented as follows.

$$p\mathrm{Cu} + q\mathrm{A} + r\mathrm{L} + s\mathrm{H} \rightleftharpoons \mathrm{Cu}_p\mathrm{A}_q\mathrm{L}_r\mathrm{H}_s$$

$$\beta_{pqrs} = \frac{[\mathrm{Cu}_p\mathrm{A}_q\mathrm{L}_r\mathrm{H}_s]}{[\mathrm{Cu}]^p[\mathrm{A}]^q[\mathrm{L}]^r[\mathrm{H}]^s} \tag{2}$$

Where, A and H denote acetate ion and hydrogen ion, and p, q, r, and s denote the numbers of Cu, A, L, and H, respectively. The coordinated water and the charge numbers of each ionic species were omitted to simplify the expression.

Hypothesizing the best model which is close to the equilibrum system in aqueous solution, the successive stability constants were calculated by the use of the SUPERQUAD computer program[6] inputted the titration data together with the values of γ_H, K_w, and K_L. (The acid dissociation constants of the protonated imidazoles cation, K_L, used the values reported in the previous paper.[5])

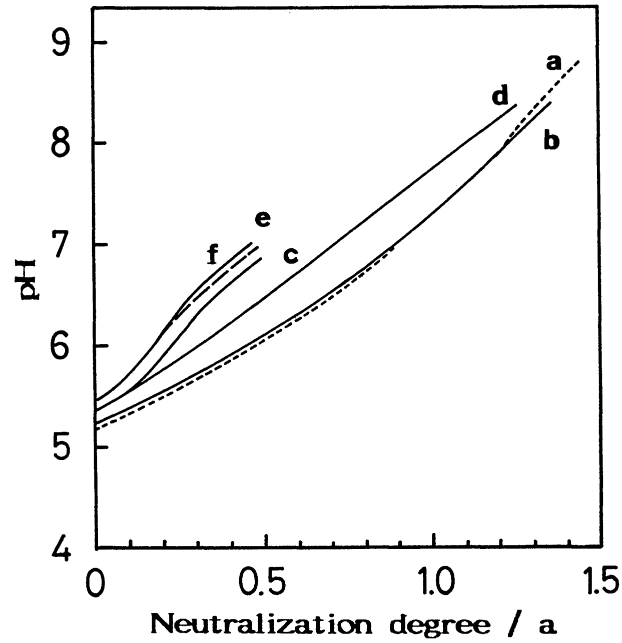

Fig. 1. Potentiometric titration curves of the $Cu(CH_3COO)_2$: L=1 : 4 system. L: HIm **a**, 1-CH_3·Im **b**, 2-CH_3·HIm **c**, 4-CH_3·HIm **d**, 2-C_2H_5·HIm **e**, 2-$(CH_3)_2CH$·HIm **f**. Concn of $Cu(CH_3COO)_2$: 9.546×10^{-4} M. Concn of L: $(3.820-4.004)\times10^{-3}$ M. Concn of CH_3COOH: 4.396×10^{-3} M. Concn of NaOH: 9.676×10^{-2} M.

Results

(1) Activity Coefficient of Hydrogen Ion and Ionic Product of Water. The average values of γ_H and K_w were 0.8073 (in the pH 3 to 5 region) and 1.334×10^{-14} (in the pH 10 to 12 region) in acetic acid solution, respectively. Hereinafter, the values of $[H^+]$ and $[OH^-]$ for some pH reading were calculated from Eq. 1 by the use of γ_H and K_w measured from the acetic acid solutions.

(2) Stability Constants. The representative titration curves shown in Fig. 1 were obtained from the solution of the 1 : 4 mole ratio of copper(II) acetate and imidazoles.

The titration was impossible to run because of the formation of copper(II) hydroxide at higher pH more than 8.5 for **a**, **b**, and **d**, and 6.5 for **c**, **e**, and **f**.

To calculate the stability constant of the complexes, the titration data obtained from the 1 : 4 mole ratio was inputted into the program together with those data obtained from the 1 : 8 and 1 : 12 mole ratios. In this case, the 2.10 was used as the stability constant (log K_{CuA}) of CuA^+.[5]

The stability constants shown in Table 1 are the average value obtained from the range of pH 5.0 to 8.5.

As the ionic species of $[CuAL_r]^+$ type, the four kinds corresponding to r=1, 2, 3, and 4 were detected from the complexes of **a**, **b**, and **d**, and the three kinds corresponding to r=1, 2, and 3, from the complexes of **c**, **e**, and **f**, respectively. From the results as mentioned above, the ionic species is conveniently classified into two groups such as Group(I) consisted of **a**, **b**, and **d**, and Group(2) consisted of **c**, **e**, and **f**.

The stability constants of the ionic species for r=1 were in good agreement with the values reported in the previous paper.[5] The stability constants of the other ionic species except for $[CuAL_4]^+$ of Group(1) indicated a slightly large value compared with those of the analogous species for Group(2).

On the other hand, the species of $[CuL_2H_s]^{(2+s)+}$ type

Table 1. Stability Constants of the Ionic Species Detected from $[Cu_pA_qL_rH_s]^{(2-q+s)+}$

L		Stability constant log β_{pqrs}				
		1110	1120	1130	1140[a)]	102−2
HIm	**a**	6.75 (0.06)	10.35 (0.07)	13.32 (0.06)	16.00 (0.08)	−7.83 (0.08)
1-CH_3·Im	**b**	6.48 (0.07)	10.03 (0.06)	12.92 (0.07)	15.65 (0.08)	−8.17 (0.09)
2-CH_3·HIm	**c**	6.31 (0.06)	9.71 (0.04)	12.83 (0.08)		−6.91 (0.12)
4-CH_3·HIm	**d**	6.44 (0.02)	9.91 (0.05)	12.89 (0.05)	15.27 (0.05)	−8.00 (0.06)
2-C_2H_5·HIm	**e**	6.15 (0.03)	9.30 (0.05)	12.18 (0.07)		−7.12 (0.10)
2-$(CH_3)_2CH$·HIm	**f**	5.73 (0.06)	8.62 (0.04)	11.35 (0.07)		−7.58 (0.11)

a) This ionic species seems to be the $[CuL_4]A^+$ type. The values in parenthesis are the standard deviations.

which indicated the value of $s=-2$, that is, hydroxo species which can be expressed by $[\mathrm{CuL_2(OH)_2}]$ is considered to be formed by the hydrolysis of ionic species consisted of **a**—**f**. The stability constants were in the range of −6.9 to −8.2 as $\log \beta_{102\text{-}2}$.

Discussion

(1) Stability of Ionic Species. 1) Influence of Acetate Ion. The stability constants for the ionic species of $[\mathrm{CuAL}_r]^+$ type indicated the higher values in the range of 2—3 as $\log \beta_{11r0}$ than those of $[\mathrm{CuL}_r]^{2+}$ (r=1, 2, 3, and 4) type reported by Nozaki et al.[9] and Sjöberg.[10] Therefore, the stability of ionic species for $[\mathrm{CuAL}_r]^+$ type was found to be increased than those of $[\mathrm{CuL}_r]^{2+}$ type because of the neutralization effect of charge by the coordination of acetate ion to copper(II).

2) Influence of Alkyl Groups. According to the X-ray crystal analysis of $[\mathrm{Cu(HIm)_4}]^{2+}$, it has been reported that the imidazole ring is inclined at angle of 72.4° from the $\mathrm{CuN_4}$ plane.[11] Then, the imidazole ring of ionic species consisted of the alkylimidazoles is presumed to be inclined at more than 72.4° because of the steric hindrance between alkyl group and acetate ion or between each alkyl group. Therefore, the stability constants of ionic species for the alkylimidazoles–copper(II) complexes shown in Table 1 indicated a slightly small value than those of ionic species for a imidazole–copper(II) complex.

The stability constants of these ionic species decreased in the order of **b**(1-substituted)⩾**d**(4-substituted)>**c**(2-substituted) relating to the position of methyl group, and **c**(2-CH_3)>**e**($2\text{-C}_2\text{H}_5$)>**f**($2\text{-(CH}_3)_2\text{CH}$) relating to the kinds of alkyl group substituted at 2-position, respectively. The former is considered to be agreed with the order of the increase of steric hindrance. The latter is in agreement with the order of the polar substituent constant for the aliphatic series,[12] and is also considered to be agreed with the order of bulkiness for the alkyl groups.

The order of stability constants for the hydroxo species could not to be found the similar tendency with that for the ionic species. This reason is considered to be due to the different of the steric hindrance on hydroxide ion and acetate ion.

To investigate the stability of ionic species, we were discussed from the term of $\Delta\log K_r$ shown in Eq. 3.

$$\begin{aligned} \Delta\log K_r &= \Delta\log \beta_{11r0} - \log K_{\mathrm{CuA}} \quad (r=1) \\ \Delta\log K_r &= \Delta\log \beta_{11r0} - \log K_{11(r-1)0} \quad (r=2,\ 3,\ \text{and } 4) \end{aligned} \tag{3}$$

These values are given in Table 2.

The $\Delta\log K_r$ of these ionic species for Group(1) indicated a slightly large value as compared with those of ionic species of the same type for Group(2). The magnitude of $\Delta\log K_r$ suggests the difficulty or facility of introduction of the rth ligand into the $[\mathrm{CuAL}_{(r-1)}]^+$ species. The $\Delta\log K_r$ of each ionic species tend to decrease in the order of the r=1, 2, 3, and 4. Such result suggests that the introduction of ligand of rth into $[\mathrm{CuAL}_{(r-1)}]^+$ species is made gradually difficult with the increase of numbers of r.

From the stability constants and the $\Delta\log K_r$, the stability of ionic species is summarized as follows.

(1) The ionic species consisted of **a** no having the substituent on the imidazole ring indicate the slightly high stability than those of **b**—**f**.

(2) As the ionic species consisted of **b**, **c**, and **d** do not suffer excessively the influence of steric hindrance on the position of methyl group bonded to the imidazole ring, the stability of these ionic species is similar to each other.

(3) The stability of the ionic species consisted of **c**, **e**, and **f** having the alkyl group on the 2-position of imidazole ring tends to decrease with the increase of bulkiness of the alkyl group.

(4) The ionic species consisted of **f** having the bulky alkyl group indicate the low stability than those consisted of **a**—**e**.

As mentioned above, the stability of imidazoles–copper(II) complexes is explained from the steric effect caused by the alkyl group.

(2) Distribution Curves of Complex Species. The distribution state of the ionic species and hydroxo species were investigated from the stability constants as a function of pH. These results are shown in Fig. 2.

The ionic species of $[\mathrm{CuAL}_r]^+$ types were found to form in the order of r=1, 2, 3, and 4 with the increase of pH. The hydroxo species of $[\mathrm{CuL_2(OH)_2}]$ type, which formed by the hydrolysis of these ionic species, was detected at pH more than 6.5, and its amounts increased rapidly with pH.

The distribution curves of these ionic species are classified into the two patterns of Group(1) and Group(2) as described already. On the basis of this classification,

Table 2. Values of $\Delta\log K_r$ for Each Ionic Species

r	Group (1)			Group (2)		
	HIm **a**	$1\text{-CH}_3\text{·Im}$ **b**	$4\text{-CH}_3\text{·HIm}$ **d**	$2\text{-CH}_3\text{·HIm}$ **c**	$2\text{-C}_2\text{H}_5\text{·HIm}$ **e**	$2\text{-(CH}_3)_2\text{CH·HIm}$ **f**
1	4.65	4.38	4.34	4.21	4.05	3.63
2	3.60	3.55	3.74	3.40	3.15	2.89
3	2.97	2.89	2.98	3.12	2.88	2.73
4	2.68	2.73	2.38			

Table 3. The pH and the Percentage of Ionic Species at the Maximum Point of Distribution Curves

Ionic species	Group		Maximum point *r* 1	2	3	4
$[CuAL_r]^+$	(1) **a**, **b**, **d**	pH	5.6—6.3	6.4—7.1	7.3—7.7	7.6—7.9
		%	42—50	42—47	32—36	8—22
	(2) **c**, **e**, **f**	pH	6.7—6.9	7.1—7.2	7.3—7.4	
		%	25—38	7—25	4—12	

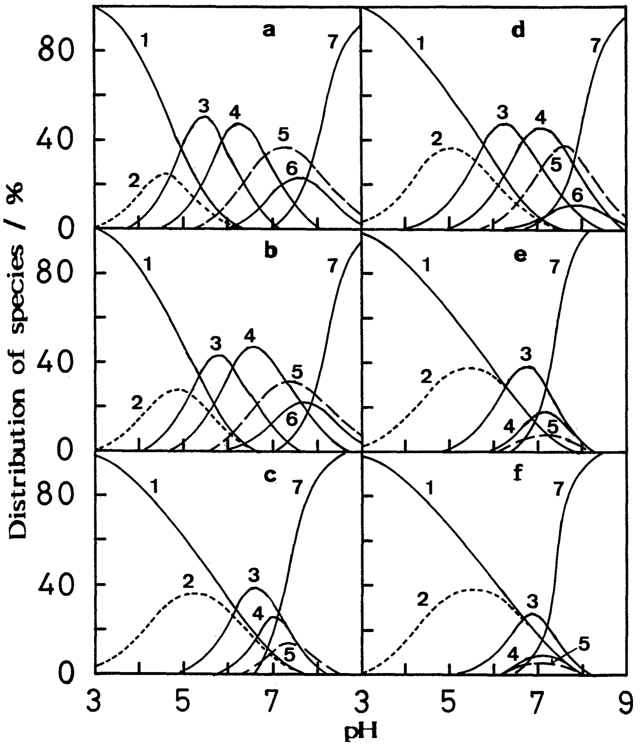

Fig. 2. Distribution curves of the $[CuA_qL_rH_s]^{(2-q+s)+}$ species obtained from the $Cu(CH_3COO)_2$:L=1:4 system. L: Same as Fig. 1. Concn of $Cu(CH_3COO)_2$, L and CH_3COOH: Same as Fig. 1. 1: $q=r=s=0$, 2: $q=1$ $r=s=0$, 3: $q=r=1$, $s=0$, 4: $q=1$ $r=2$ $s=0$, 5: $q=1$ $r=3$ $s=0$, 6: $q=1$ $r=4$ $s=0$, 7: $q=0$ $r=2$ $s=-2$.

the relationship between the pH and the percentage at the maximum point of each ionic species were summarized in Table 3.

The ionic species of $r=1$ and 2 detected from the complexes belong to Group(1), and $r=1$ detected from the complexes belong to Group(2) were ascertained to be preferentially formed in the acidic regions. Additionally, the ionic species of $[CuA]^+$ was present over a wide range of pH, and its maximum point of distribution was 24—35% at pH 4.7—5.6. On the other hand, the ionic species of $r=3$ and 4 detected from the complexes belong to Group(1), and $r=2$ and 3 detected from the complexes belong to Group(2) were ascertained mainly to be formed in the basic regions, respectively.

These ionic species were hydrolyzed with increase of pH, and were found to be changed to the hydroxo species of $[CuL_2(OH)_2]$ type.

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