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A Potentiometric Study on Mixed Ligand Cadmium(II) Complexes with 2-Amino Carboxylic Acids

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Formation constants of mixed ligand cadmium(II) complexes, CdLL′, were determined in aqueous solutions containing 3 mol dm^{-3} $LiClO_4$ as a constant ionic medium at 25 °C by potentiometric titration, where the ligands HL and HL′ are 2-amino carboxylic acids such as glycine, α-alanine, 2-aminobutanoic acid, 2-aminopentanoic acid, and 2-aminohexanoic acid. Ten kinds of the mixed ligand cadmium(II) complexes were examined with the combination of five 2-amino carboxylic acids. The formation constant, $\beta_{prs}=[Cd_pL_rL'^{(2p-r-s)+}_s]/([Cd^{2+}]^p\times[L^-]^r[L'^-]^s)$, of the mixed ligand cadmium(II) complexes containing glycine as one of the ligands lie between those of the parent complexes, while the formation constants of the other complexes are larger than those of the parent complexes. No protonated mixed ligand complex has been observed. The small values of β_{111} of the Cd(gly)L complexes are due to the considerably small values of the first stepwise formation constants of the CdL^+ complexes. On the other hand, the stepwise formation constants of the CdL^+ complexes with glycinate ion are larger than the stepwise formation constants with 2-amino carboxylate ions and the second stepwise constant of the bis(glycinato)cadmium(II) complex. Interactions between the ligands through the central cadmium(II) ion are discussed. The *b*-values ($b=\log\{(K_{110}\cdot K_{101})/(K_{120}\cdot K_{102})\}$, where K_{1rs} denotes the stepwise formation constant of the complex $CdL_rL'_s$) of the mixed ligand cadmium(II) complexes containing glycinate ion as one of the components lie between 0.93 and 0.98, and are larger than those of the other complexes (b=0.83—0.90), the fact indicating that the mixed ligand glycinato complexes have larger inter-ligand interactions within the complexes than those within complexes containing other 2-amino carboxylate ions. The inter-ligand interaction may occur through the central cadmium ion within the complex.

Mixed ligand complexes of a number of metal ions with various amino acids have been extensively investigated because of their biological importance, and the role of the metal ions in the mixed ligand complexes in various reactions has been discussed. Among them, copper(II) complexes are the most extensively studied ones, and zinc(II) complexes have also drawn attentions of chemists due to their interesting behavior in catalytic reactions in biological systems. Cadmium(II) ions often show similar properties in chemical reactions to zinc(II) ions because of their similar electron configurations (d^{10} electrons).[1] However, mixed ligand amino acido complexes of cadmium(II) ion have scarecely been examined so far. Toxity of cadmium(II) ion is an important problem to be elucidated in the view-point of medical science, as well as of complex chemistry. Reactions of cadmium(II) ions with amino acids which exist in human plasma[2] and other biological tissues and organs, therefore, are worthwhile studying in connection of complex chemistry of cadmium(II) ions with biochemistry.

The aim of the present work is to determine formation constants of mixed ligand complexes of cadmium(II) ion with a series of 2-amino carboxylic acids, such as glycine, α-alanine, 2-aminobutanoic acid, 2-aminopentanoic acid and 2-aminohexanoic acid, and variations of the formation constants of the mixed ligand complexes are discussed in terms of the effect of substituted alkyl groups at the carbon atom of glycine.

The effect of the size of chelate rings of amino acids in the complexes on formation constants of various mixed ligand complexes has also been examined by using 3- and 4-amino carboxylic acids, but the complexes of cadmium(II) ions with the acids are so weak that the complexes are not practically formed.

Experimental

Reagents. The amino acids were obtained from Wako Pure Chemicals Ind., Osaka, Nakarai Chemicals Co., Kyoto, and Katayama Chemicals Ind., Osaka. Each reagent was purchased from at least two different companies and purity of the reagents was checked by paper chromatography. A reagent having better quality was chosen, and then, it is recrystallized and used after drying crystals for several hours at 90—110 °C in an electric oven. Cadmium perchlorate, lithium perchlorate and lithium hydroxide were prepared by the methods as described in previous papers.[3,4]

Apparatus. Beckman (Nos. 40495 and 40498) glass electrodes were used in combination with an Orion Digital pH Meter 801. The Kawai-type half cell[5] was used, in which an Ag–AgCl electrode was set. The Ag–AgCl electrode was prepared according to Brown.[6]

Measurements. During potentiometric titrations the total concentration of perchlorate ions was kept constant at 3 mol dm^{-3} by using lithium perchlorate. The ratio of the total concentration of ligands (the sum of the concentrations of two amino acids) to that of cadmium(II) ions (C_L^t/C_{Cd}^t) was 5 in all the cases. The total concentration of amino acids in the solution (C_L^t) was changed, but the ratio of the concentrations of each amino acid was kept 1 : 1. The method of emf measurements was essentially the same as that employed in the previous work.[3,4]

All the measurements were carried out under a nitrogen atomosphere at 25.00±0.02 °C in a liquid paraffin bath set in a room thermostated at 25.0±1.5 °C.

Results

Typical results of titration curves of the systems of cadmium(II)–amino acids are shown in Fig. 1, in which the degree of neutralization of the total amino acids in the solutions X ($=-\boldsymbol{H}/C_L^t$; $\boldsymbol{H}$ stands for the analytical

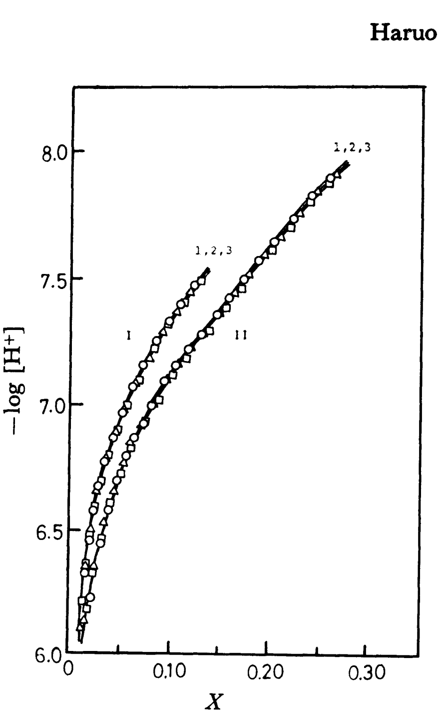

Fig. 1. Typical titration curves of cadmium(II)–amino acid mixed solutions.
Curve I (Cd(II)–2-aminobutanoic acid–2-aminopentanoic acid):
1 (○), C_{cd}(mmol dm^{-3}) = 7.524, C_{L}(mmol dm^{-3}) = 18.71, C_{L}' (mmol dm^{-3}) = 18.71; 2 (△), 7.793, 19.36, 19.35; 3 (□), 7.847, 19.62, 19.59.
Curve II (Cd(II)–glycine–2-aminobutanoic acid): 1 (○), 7.571, 18.80, 18.81; 2 (△), 7.771, 19.38, 19.38; 3 (□), 8.139, 20.39, 20.37.

excess concentration of hydrogen ion) was plotted against −log [H$^+$]. The least squares method was employed to determine the best value of the formation constant of a mixed ligand complex, CdLL′, by taking into account the formation constants of the parent cadmium(II) complexes with each amino acid as the component, which had been determined by separate experiments using solutions containing cadmium(II) ions and one kind of amino acid as a ligand. The formation constants of the mixed ligand complexes $\beta_{pqrs}=[\mathrm{Cd}_p\mathrm{H}_q\mathrm{L}_r\mathrm{L}'_s]^{(2p+q-r-s)+}/([\mathrm{Cd}^{2+}]^p[\mathrm{H}^+]^q[\mathrm{L}^-]^r[\mathrm{L}'^-]^s)$ are summarized in Table 1, together with the ionization constants of the ligands (pK_1 and pK_2) and the formation constants of mono- and bis-complexes with one kind of amino acid as the ligand (log K_{11} and log K_{12}). Neither the protonated complexes nor the tris(amino acido)cadmium(II) complexes have been found with reliable accuracies under the present experimental conditions. The values of K_{11} and K_{12} are refined ones which had been determined,[7] the refinement being done for eliminating titration data at higher pH regions where white precipitates sometimes appeared. The formation of hydroxo complexes of cadmium ions[8] has been taken into consideration in the course of the least squares refinement of the formation constants of the mixed ligand complexes. The calculations were carried out by using the SCOGS program[9] with an electronic computer FACOM M-160S.

The solid lines in Fig. 1 were drawn using calculated values of X (X_{calcd}) by the following equation:

$$X_{\mathrm{calcd}} = \frac{C_{\mathrm{L}}^{\mathrm{t}} + K_i[\mathrm{H}^+]^{-1} - [\mathrm{H}^+] - \sum_p\sum_q\sum_r\sum_s q\beta_{pqrs}[\mathrm{Cd}^{2+}]^p[\mathrm{H}^+]^q[\mathrm{L}^-]^r[\mathrm{L}'^-]^s}{C_{\mathrm{L}}^{\mathrm{t}}}, \tag{1}$$

where K_i represents the autoprotolysis constant of water in 3 mol dm^{-3} LiClO$_4$ aqueous solution at 25 °C ($10^{-13.87}$ mol^2 dm^{-6} [10]). Under the present conditions, the values of p, q, r, and s for the mixed ligand cadmium(II) complexes are 1, 0, 1, and 1, respectively. The formation of the CdOH$^+$ (p=1, q=−1, r=s=0) and Cd$_2$OH^{3+} (p=2, q=−1, r=s=0) complexes[8] has been taken into account in the determination of formation constants of the mixed ligand complexes, β_{pqrs}, by using Eq. 1. Since only the 1 : 1 : 1 type mixed ligand complexes without protons (p=1, q=0, r=1, s=1) have been found in the present work, the formation constants of the mixed ligand complexes will be simply denoted as β_{1rs} (*e.g.*, β_{111} for a 1 : 1 : 1 mixed complex).

TABLE 1. FORMATION CONSTANTS OF CADMIUM(II) COMPLEXES WITH 2-AMINO CARBOXYLIC ACIDS IN 3 mol dm^{-3} LiClO$_4$ AT 25 °C

		Glycine	α-Alanine	2-Amino-butanoic acid	2-Amino-pentanoic acid	2-Amino-hexanoic acid
a) Ionization constants of 2-amino carboxylic acids.						
pK_1		2.76	2.81	—	—	—
pK_2		9.68	9.72	9.73	9.75	9.76
b) Formation constants of mono- and bis(2-amino carboxylato)cadmium(II) complexes.						
log K_{11}		4.01	3.69	3.64	3.72	3.74
log K_{12}		3.48	3.24	3.24	3.29	3.29
c) Formation constants of mixed ligand complexes of cadmium(II) ion.[a]						
log β_{111}	Glycine	$\underline{7.49}$	7.47	7.34	7.41	7.43
	α-Alanine		$\underline{6.93}$	7.13	7.15	7.24
	2-Aminobutanoic acid			$\underline{6.88}$	7.05	7.20
	2-Aminopentanoic acid				$\underline{7.01}$	7.31
	2-Aminohexanoic acid					$\underline{7.03}$

a) Values underlined are log β_{120} or log β_{102} (=log K_{11}+log K_{12}). Standard deviations are ±0.02.

Protonation reactions of mono- and bis(amino acido)-cadmium(II) complexes have not been observed under the present experimental conditions.

It should be noted from the results in Table 1 that the values of pK_1 and pK_2 are increased, whereas the values of log K_{11} and log K_{12} are decreased, by introducing alkyl groups to glycine, where K_{11} and K_{12} represent the stepwise formation constants of the CdL$^+$ and CdL$_2$ complexes, respectively.

Discussion

The formation constant of a mixed ligand complex should be larger than the average value of the formation constants of the parent complexes by a statistical factor as long as the bond strength between the central metal ion and the ligands is unaffected by replacing a ligand with another one and the contribution of entropy changes in each reaction to the formation constants are the same.

In the formation of a 1 : 1 : 1 mixed ligand complex CdLL′ from the parent bis-complexes, CdL$_2$ and CdL′$_2$, the statistical factor is 4.

The formation reaction of the mixed ligand CdLL′ complex from the parent complexes can be described as follows:

$$\mathrm{CdL_2} + \mathrm{CdL'_2} = 2\mathrm{CdLL'}. \qquad (2)$$

The formation constants of the mixed ligand complex β_{111} are related to the formation constants of the parent CdL$_2$ and CdL′$_2$ complexes, β_{120} and β_{102}, respectively, by the following equation:

$$2 \log \beta_{111} = \log \beta_{120} + \log \beta_{102} + \log F_{\mathrm{m}}. \qquad (3)$$

F_{m} is 4 in the ideal case.

For most mixed ligand complexes examined here, β_{111} is larger than β_{120} and β_{102}. However, as we can see from Table 1c, the formation constants of the mixed ligand complexes containing glycinate ion as one component lie between the values of the two parent complexes, thus, $\beta_{120} > \beta_{111} > \beta_{102}$, although the relationship $\beta^2_{111} > \beta_{120} \cdot \beta_{102}$ still holds for the complexes.

The second stepwise formation constants K^{m}_{12} of the mixed ligand complexes in the reaction

$$\mathrm{CdL^+} + \mathrm{L'^-} = \mathrm{CdLL'} \qquad (4)$$

are calculated by using the following equation:

$$\log K^{\mathrm{m}}_{12} = \log \beta_{111} - \log K_{11}. \qquad (5)$$

The values of log K^{m}_{12} are summarized in Table 2. The values of log K^{m}_{12} of the Cd(gly)L complexes with various 2-amino carboxylate anions L$^-$

$$\mathrm{CdL^+} + \mathrm{gly^-} = \mathrm{Cd(gly)L} \qquad (6)$$

are in the range of 3.69 to 3.78, which are larger than the log K_{12} value of the bis(glycinato)cadmium(II) complex. On the other hand, the log K^{m}_{12} values of the reaction

$$\mathrm{Cd(gly)^+} + \mathrm{L^-} = \mathrm{Cd(gly)L} \qquad (7)$$

fall in the range of 3.33 to 3.46, which are comparable to the values of the other complexes given in Table 2. Therefore, we see that the small values of β_{111} of the Cd(gly)L complexes are due to the considerably small values of the first stepwise formation constants of the CdL$^+$ complexes compared with those of the Cd(gly)$^+$ complex (Table 1b).

The second formation constants of the mixed ligand complexes containing glycinate ion as the second entering ligand are larger than those of other complexes, and even larger than the K_{12} value of the bis(glycinato)-cadmium(II) complex. This fact implies that glycinate ion combines more favorably with a CdL$^+$ than with the Cd(gly)$^+$ complex. Since direct interactions between glycinate and another ligand within the CdL$^+$ complex may hardly be expected, interactions between the ligands through the central metal ion should be considered.

Electrons in the highest orbitals of cadmium(II) ion which is a considerably soft acid according to classification by Ahrland, *et al.*[11] and Pearson[12] may partially delocalize over the central metal ion and the ligand atoms within the complex in order to decrease the total energy of the whole complex. Although it is generally accepted that atoms of the first and second rows of the periodic table cannot be acceptors of such electrons, we think that the possibility may not be completely excluded in cases where a central atom has electrons with very large principal quantum numbers, or in other words, it has a very soft character, because energy levels of electrons of the central metal ion and ligand atoms such as oxygen and nitrogen are so different that even small delocalization of electrons of the metal ion by using a higher orbitals of the ligand atoms may decrease, to some extent, the total energy of the system.

TABLE 2. THE SECOND STEPWISE FORMATION CONSTANTS (log K^{m}_{12}) OF THE CdLL′ COMPLEXES IN 3 mol dm^{-3} LiClO$_4$ AT 25 °C[a]

CdL[b]	L′				
	Glycinate	Alaninate	2-Amino-butanoate	2-Amino-pentanoate	2-Amino-hexanoate
Cd(gly)$^+$	3.48	3.46	3.33	3.40	3.42
Cd(ala)$^+$	3.78	3.24	3.44	3.46	3.55
Cd(but)$^+$	3.70	3.49	3.24	3.41	3.56
Cd(pen)$^+$	3.69	3.43	3.33	3.29	3.59
Cd(hex)$^+$	3.69	3.50	3.46	3.57	3.29

a) Values underlined are log K_{12} of the bis(2-amino carboxylato)cadmium(II) complexes. b) Ala : Alaninate ion, but : 2-aminobutanoate ion, pen : 2-aminopentanoate ion, hex : 2-aminohexanoate ion.

This kind of electron delocalization may easily be prevented by an increase in the charge density at the ligand atoms due, for instance, to inductive effects of substituted groups within the ligand molecules.

An interpretation of the change in the K^{m}_{12} value of the Cd(gly)L complex may thus be given in the following way: the basicity of the functional groups (amino and carboxyl groups) of glycine increases by introduction of an alkyl group to the carbon atom due to its inductive effect, and therefore, the pK_1 and pK_2 values of 2-amino carboxylic acids having alkyl groups become larger than the pK_1 and pK_2 values, respectively, of glycine (see Table 1a). The introduction of the alkyl groups thus results an increase in electron densities at the nitrogen and oxygen atoms within the amino and carboxyl groups, and it may prevent electron donation from the central cadmium(II) ion. Therefore, the affinity of the amino acid anions to cadmium(II) ion decreases, as we can see from the values of K_{110} and K_{120} of the bis(amino acido)cadmium(II) complexes smaller than the corresponding values of the bis(glycinato)cadmium(II) complex (see Table 1b). The increased charge density of the cadmium(II) ion due to the decreased electron donation to the ligand atoms may result a decreased acceptability of electron pairs from the coordinated water molecules. As the result, the $H_2O\cdots CdL^+$ bonds in the solvated CdL^+ complex weaken, and the water molecules can be easily substituted with the second ligand. Since glycinate anion has the largest acceptability (*i.e.*, the smallest electron density at the ligand atoms) among the ligands examined here for the electron donation from the cadmium(II) ion, the substitution of glycinate ion with the water molecules coordinated to the cadmium(II) ion might occur most favorably to form the strongest metal-ligand bond. Thus the K^{m}_{12} value of the reaction

$$\mathrm{CdL(H_2O)}_n^+ + \mathrm{gly}^- = \mathrm{Cd(gly)L(H_2O)}_{n-2} + 2\mathrm{H_2O} \qquad (8)$$

becomes larger than the K_{12} value of the following reaction:

$$\mathrm{Cd(gly)\ (H_2O)}_n^+ + \mathrm{gly}^- = \mathrm{Cd(gly)_2(H_2O)}_{n-2} + 2\mathrm{H_2O}. \qquad (9)$$

The statistical factors log F_{m} defined by Eq. 3 for various mixed ligand complexes are summarized in Table 3, but no systematic trend of the values can be found.

Another relationship

$$\log \beta_{111} = \log \beta_{110} + \log \beta_{101} + \log F'_{\mathrm{m}} \qquad (10)$$

TABLE 3. VALUES OF log F_{m}, F'_{m}, AND b IN EQS. 3, 10, AND 13, RESPECTIVELY

Exptl No.	Complex	log F_{m}	log F'_{m}	b
1	Cd(gly)(ala)	0.52	−0.23	0.98
2	Cd(gly)(but)	0.31	−0.31	0.93
3	Cd(gly)(pen)	0.32	−0.32	0.96
4	Cd(gly)(hex)	0.34	−0.32	0.98
5	Cd(ala)(but)	0.45	−0.20	0.85
6	Cd(ala)(pen)	0.36	−0.26	0.88
7	Cd(ala)(hex)	0.52	−0.19	0.90
8	Cd(but)(pen)	0.21	−0.31	0.83
9	Cd(but)(hex)	0.49	−0.18	0.85
10	Cd(pen)(hex)	0.58	−0.15	0.88

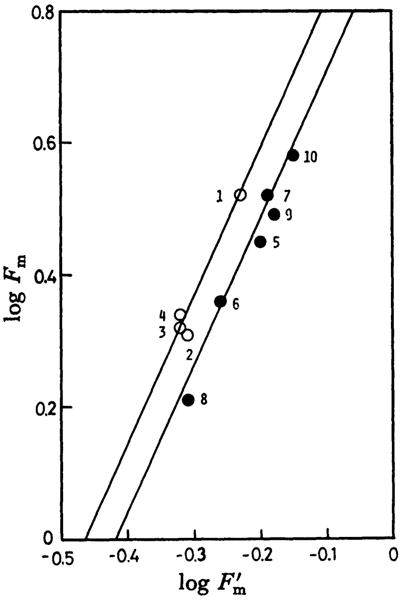

Fig. 2. The relationship between log F_{m} and log F_{m}'. ○: Mixed ligand cadmium(II) complexes containing glycinate ion, ●: other mixed ligand cadmium(II) complexes. The numbers given in the figure correspond to those of the complexes in Table 3.

is obtained for the formation of the CdLL′ complex from the parent CdL^+ and CdL'^+ complexes as follows:

$$\mathrm{CdL^+} + \mathrm{CdL'^+} = \mathrm{CdLL'} + \mathrm{Cd^{2+}}. \qquad (11)$$

F'_{m} is 2 in the ideal case. The values of log F'_{m} found are summarized in Table 3. Since the following relationship holds between F_{m} and F'_{m}

$$\log F_{\mathrm{m}} = 2 \log F'_{\mathrm{m}} + b, \qquad (12)$$

where

$$b = \log\{(K_{110}\cdot K_{101})/(K_{120}\cdot K_{102})\} \qquad (13)$$

plots of log F_{m} against log F'_{m} should give straight lines as we can see in Fig. 2. The experimental points fell on the two straight lines with a slope 2. The open circles show the mixed ligand complexes containing glycinate ion and the closed circles show the complexes not containing glycinate ion. The b-values found from the plots are given in Table 3, which should be zero in the ideal case. The b-values of the mixed ligand glycinato complexes are obviously larger than those of the other complexes, the fact indicating that the inter-ligand interactions within the mixed ligand glycinato complexes are larger than those of other complexes.

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