3458 BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 3458—3462 (1973) [Vol. 46, No. 11

Mixed Ligand Complex Formation between Monodentate Ligands and Various Tridentate Ligand-Copper(II) Complexes

Osamu Yamauchi, Hiroshi Benno, and Akitsugu Nakahara

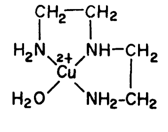
Institute of Chemistry, College of General Education, Osaka University, Toyonaka, Osaka 560

(Received June 29, 1973)

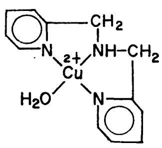
Formation of mixed ligand complexes between monodentate ligands (L) and copper(II) complexes of tridentate ligands (A) has been investigated by potentiometric titration and thermal analysis. Thus, the constants, log K_m, for the formation of the complexes of type CuA·L from CuA and L have been calculated from the titration curves by the method of non-linear least-squares. A refers to diethylenetriamine, dipicolylamine, 2,2′,2″-terpyridine, ethylenediamine-*N*-monoacetic acid, iminodiacetic acid, or pyridine-2,6-dicarboxylic acid and L to pyridine, *p*-phenolsulfonic acid, *n*-butylamine, or hydroxy group. The stability series in each system with L fixed has been interpreted in terms of the strength of A as a Lewis base, expressed by the sum of pK_a ($\sum pK_a$), as well as back-donation. In the absence of significant steric hindrance, favorable combination of donor atoms around copper(II) has been found to be between aromatic nitrogens and negative oxygens. Thermal stability of the isolated complexes of type CuA·PY, where PY is pyridine, was also in line with the stability sequence in solution.

Recent interest in the mechanisms of the biological reactions involving metal ions as central atoms has prompted a variety of basic studies on mixed ligand metal complexes. Sigel *et al.*[1–3] investigated systematically the complex formation between copper(II)-2,2′-bipyridine and oxygen- and/or nitrogen-containing bidentate ligands, and gave explanations to the affinity and the driving force leading to mixed ligand complexes.

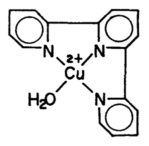
It seems reasonable to assume that, in the course of a biological reaction, the central metal ion is surrounded by a multidentate ligand, leaving only one coordination site available for the second ligand. In this connection, Angelici and Allison[4] reported the mixed complex formation between substituted diethylenetriamine complexes of copper(II) and several amino acids which coordinate as bidentate ligands, and Hauer *et al.*[5] reported the reactions of polyamines with copper(II)-triglycine. However, it is of further interest to study the coordination of purely monodentate ligands to copper(II) complexes of tridentate ligands of different types.



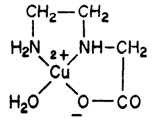
Cu(dien)



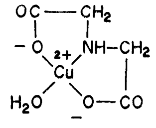
Cu(dpa)



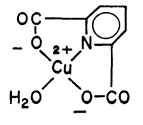
Cu(terpy)



Cu(edma)



Cu(ida)



Cu(pdca)

In order to find out the effects of combination of two ligands around copper(II) on the stability of the resulting mixed ligand complex, we investigated the complex formation of pyridine (PY), *p*-phenolsulfonic acid (PPS), and *n*-butylamine (BA) with the copper(II) complexes of diethylenetriamine (Cu(dien)), dipicolylamine (Cu(dpa)), 2,2′,2″-terpyridine (Cu(terpy)), ethylenediamine-*N*-monoacetic acid (Cu(edma)), iminodiacetic acid (Cu(ida)), and pyridine-2,6-dicarboxylic acid (Cu(pdca))[6] by potentiometric titration and thermal analysis.

Experimental

Materials. *Copper(II) Complexes*: The binary complexes (CuA) used are Cu(dien)$(NO_3)_2$, Cu(dpa)Cl_2, Cu(terpy)$(ClO_4)_2 \cdot H_2O$, Cu(edma)Cl, Cu(ida)$\cdot 2H_2O$, and Cu(pdca)$\cdot 2H_2O$, all of which were prepared from equal amounts of a ligand and an appropriate salt of copper(II) in water or aqueous ethanol.

Mixed ligand complexes of type CuA·PY, where A is dien, terpy, ida, or pdca, were obtained by recrystallizing the binary complexes from aqueous pyridine. The relevant elemental analysis data are summarized in Table 1.

Ligands: Pyridine and *n*-butylamine were converted to the perchlorates, which were purified by recrystallization from water. Sodium *p*-phenolsulfonate was purchased from Nakarai Chemicals Co., and recrystallized from water.

All the other chemicals used were of reagent grade, distilled and deionized water being used.

pH Titrations. *(a) Reagents*: 0.1 M KOH was prepared according to Albert,[7] and stored under a nitrogen atmosphere. 0.01 M $Cu(NO_3)_2$ was prepared by dissolving copper(II) nitrate trihydrate in water and standardized against standard zinc by chelatometric titration.[8]

---

[1] R. Griesser and H. Sigel, *Inorg. Chem.*, **9**, 1238 (1970); *ibid.*, **10**, 2229 (1971). Also, the papers cited therein.

[2] P. R. Huber, R. Griesser, and H. Sigel, *ibid.*, **10**, 945 (1971).

[3] H. Sigel, P. R. Huber, and R. F. Pasternack, *ibid.*, **10**, 2226 (1971).

[4] R. J. Angelici and J. W. Allison, *ibid.*, **10**, 2238 (1971).

[5] H. Hauer, E. J. Billo, and D. W. Margerum, *J. Amer. Chem. Soc.*, **93**, 4173 (1971).

[6] These binary complexes will be abbreviated as CuA in the text hereinafter. Mixed complexes of CuA with the second ligand L will generally be described as CuA·L, where L is pyridine (PY), *p*-phenolsulfonate (PPS), *n*-butylamine (BA), or hydroxy group (OH). Thus, the complex of Cu(dien) with pyridine is expressed as Cu(dien)·PY. All the charges are omitted for simplicity.

[7] A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," Methuen and Co., Ltd., London (1962).

[8] K. L. Cheng, *Anal. Chem.*, **30**, 243 (1958).

Table 1. Elemental analysis of CuA and CuA·PY

Complex[a]	Elemental analysis					
	C (%)		H (%)		N (%)	
	Calcd	Found	Calcd	Found	Calcd	Found
[Cu(dien)NO_3]NO_3	16.52	16.33	4.51	4.43	24.08	24.27
[Cu(dpa)Cl]Cl	43.19	43.30	3.93	3.78	12.59	12.43
[Cu(terpy)H_2O]$(ClO_4)_2$	35.05	35.09	2.55	2.43	8.18	8.25
[Cu(edma)Cl]	22.23	22.22	4.20	4.15	12.96	13.17
[Cu(ida)H_2O]·H_2O	20.82	20.85	3.93	3.93	6.07	6.15
[Cu(pdca)H_2O]·H_2O	31.77	31.91	2.67	2.79	5.29	5.31
[Cu(dien)PY]$(NO_3)_2$	29.21	29.12	4.90	4.90	22.71	22.82
[Cu(terpy)PY]$(ClO_4)_2$	41.81	41.75	2.81	2.11	9.75	9.55
[Cu(ida)PY]	39.47	39.77	3.69	3.34	10.23	10.36
[Cu(pdca)PY]	46.82	47.25	2.62	2.50	9.11	9.26

a) The complexes are tentatively expressed by assuming that copper(II) is four-coordinate.

(b) Apparatus: A Radiometer PHM 4d pH meter with a G202B glass electrode and a K401 calomel electrode was used after standardization with a Horiba standard buffer solution (pH 4.01).

(c) Procedure: Titrations were carried out at concentrations of 4×10^{-3}—8×10^{-3} M in water (μ=0.1(KNO_3)) at 25 °C under a nitrogen atmosphere. Details of the procedure were essentially the same as before,[9] and conversion of pH to -log [H^+], where [H^+] denotes the hydrogen ion concentration, was done in the manner described.[9]

Measurement of Absorption Spectra. The absorption spectra of various mixtures of Cu(dien) and pyridine (10^{-2}—10^{-3} M) were measured in water at pH 7.0 with a Shimadzu MPS 50L recording spectrophotometer.

Measurement of Thermal Stability. The thermal stabilities of the mixed ligand complexes were measured with a Rigaku Denki Thermoflex No. 8001, the rate of temperature elevation being 5 °C per minute.

Results and Discussion

Typical titration curves of the complexes CuA in the presence of the equimolar amounts of pyridine, *p*-phenolsulfonate, and *n*-butylamine are shown in Figs.

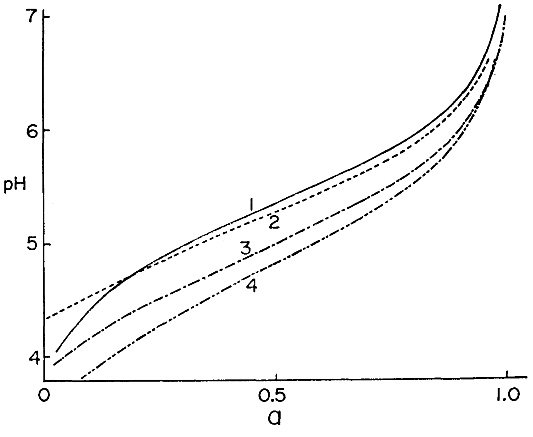


Fig. 1. Titration curves of pyridine in the presence and the absence of CuA. *a* is moles of KOH added per mole of ligand.
1, PY alone; 2, Cu(dien): PY=1: 1; 3, Cu(ida): PY=1: 1; 4, Cu(pdca): PY=1: 1.

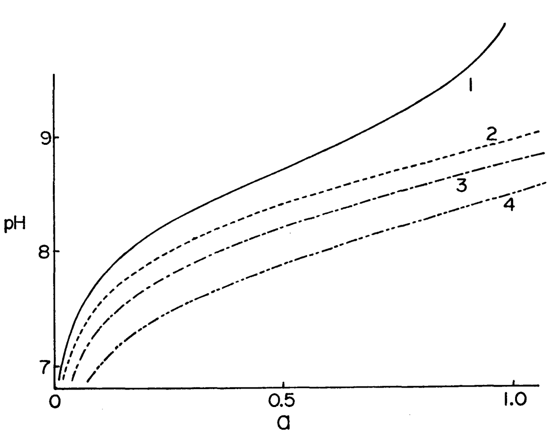


Fig. 2. Titration curves of *p*-phenolsulfonate in the presence and the absence of CuA.
1, PPS alone; 2, Cu(dien): PPS=1: 1; 3, Cu(dpa): PPS=1: 1; 4, Cu(terpy): PPS=1: 1.

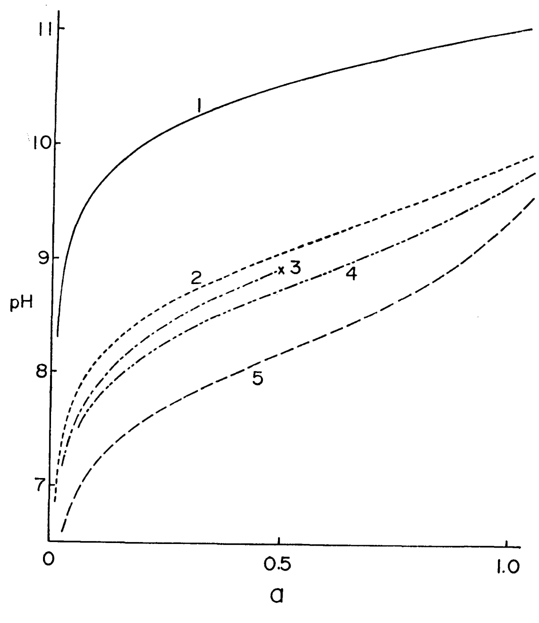


Fig. 3. Titration curves of *n*-butylamine in the presence and the absence of CuA.
1, BA alone; 2, Cu(dien): BA=1: 1; 3, Cu(edma): BA=1: 1; 4, Cu(dpa): BA=1: 1; 5, Cu(terpy): BA=1: 1.

---

[9] O. Yamauchi, H. Miyata, and A. Nakahara, This Bulletin, **44**, 2716 (1971).

1, 2, and 3, respectively. The pH decrease due to the presence of CuA indicates mixed ligand complex formation in these systems. There seems to be protonation of A in the CuA·PY series at pH below 5, whereas formation of the hydroxy complexes should be taken into account for CuA·PPS and CuA·BA systems which lack the pH jump at $a=1.0$. Cu(ida)·L and Cu(pdca)·L systems, where L=*p*-phenolsulfonate or *n*-butylamine, did not afford reliable titration curves owing to precipitation.

The absorption spectra of Cu(dien)·PY system at various Cu(dien): pyridine ratios in water at pH 7.0 showed the isosbestic point at 635 nm, which indicates the following reaction is the only one around this pH (charges are omitted for simplicity):

$$\mathrm{Cu(dien)} + \mathrm{PY} \rightleftharpoons \mathrm{Cu(dien)\cdot PY}$$

This is also confirmed by the compositions of the mixed ligand complexes isolated as crystals.

From these observations, we assumed the following equilibria for the mixed ligand systems with the constants defined:

$$\mathrm{HL} \xrightleftharpoons{K_a} \mathrm{H} + \mathrm{L} \tag{1}$$

$$K_a = \frac{[\mathrm{H}][\mathrm{L}]}{[\mathrm{HL}]}$$

$$\mathrm{CuA} + \mathrm{L} \xrightleftharpoons{K_m} \mathrm{CuA\cdot L} \tag{2}$$

$$K_m = \frac{[\mathrm{CuA\cdot L}]}{[\mathrm{CuA}][\mathrm{L}]}$$

where HL refers to protonated monodentate ligand, and K_a and K_m are the acid dissociation constant and the stability constant, respectively. Dissociation of CuA to Cu and A (free tridentate ligand) may safely be neglected in the pH range investigated. The equilibria (3) and (4) were also considered at low and high pH, respectively:

$$\mathrm{CuA\cdot H} \xrightleftharpoons{K_H} \mathrm{CuA} + \mathrm{H} \tag{3}$$

$$K_H = \frac{[\mathrm{CuA}][\mathrm{H}]}{[\mathrm{CuA\cdot H}]}$$

$$\mathrm{CuA} + \mathrm{OH} \xrightleftharpoons{K_{OH}} \mathrm{CuA\cdot OH} \tag{4}$$

$$K_{OH} = \frac{[\mathrm{CuA\cdot OH}]}{[\mathrm{CuA}][\mathrm{OH}]}$$

where CuA·H and CuA·OH refer respectively to protonated and hydroxy complex.

The equilibrium constants K_H, K_{OH}, and K_m were calculated on the basis of the mole balances for total CuA and total L, and the electroneutrality of solution. Computation of the constants was made by the method of non-linear least-squares with the use of a NEAC 2200/500 computer, the program and the conditions for convergence being essentially the same as those reported.[9,10] Table 2 shows the calculated equilibrium constants along with the pK_a values of ligands A taken from the literature. The pK_H ($-\log K_H$) values for Cu(dpa), Cu(terpy), and Cu(pdca) are as low as 1.2—1.6 with large variances (>1) and not reliable. The constants K_{OH} were calculated from the data for *n*-butylamine and *p*-phenolsulfonate, for which hydrolysis was evident from the titration curves, and the values from the two systems agreed with each other to within 0.3 log unit. The log K_{OH} value of 4.75 for Cu(dien)·OH is in good agreement with the reported values of 4.58[11] and 5.17.[12]

The theoretical titration curves calculated by these constants coincided very well with the experimental ones, and the differences expressed in titer were less than 0.01 ml over the entire ranges (usually 0.2—1.0 ml).

The mixed complexes of pyridine with Cu(dien), Cu(dpa), and Cu(terpy), containing donor nitrogens only, have lower stability than the complexes with Cu(edma), Cu(ida), and Cu(pdca), suggesting that negative oxygens at the coordination sites increase the stability of the resulting complexes. According to Tanaka, the log K_m values can be calculated by a general equation derived from mechanistic considerations, and the experimental values for Cu(dien), Cu(dpa), Cu(edma), and Cu(ida) could be reproduced satisfactorily by the equation.[13]

TABLE 2. EQUILIBRIUM CONSTANTS OF CuA·L SYSTEMS (25±0.05 °C; $\mu=0.1$ ($\mathrm{KNO_3}$))[a]

CuA	$\sum$pK_a[b]	pK_H	log K_m L[c] PY	PPS	BA	log K_{OH}[g]
Cu(dien)	23.41[d]	3.24±0.12	1.77±0.09	1.72±0.27	3.49±0.15	4.75±0.12
Cu(dpa)	11.02[e]	<2	1.76±0.09	2.37±0.09	3.76±0.27	5.11±0.06
Cu(terpy)	6.97[d]	<2	1.81±0.06	2.71±0.12	4.71±0.09	5.67±0.06
Cu(edma)	18.95[f]	3.19±0.06	2.09±0.01	1.75±0.27	4.09±0.15	4.77±0.09
Cu(ida)	12.03[d]	2.67±0.15	2.65±0.02			
Cu(pdca)	6.78[d]	<2	2.97±0.02			

a) Variances are three times the estimated standard deviations.

b) The $\sum$ pK_a value is the sum of three constants of each ligand except terpy, ida, and pdca where the first dissociation constants are negligibly small.

c) The pK_a values determined in the present study are: PY, 5.26±0.03; PPS, 8.66±0.03; BA, 10.62±0.09. The value of 13.88 was used for the apparent ion product of water (pK_w').

d) L. G. Sillén and A. E. Martell, "Stability Constants of Metal-Ion Complexes," Special Publication No. 17, The Chemical Society, London (1964).

e) J. K. Romary, J. D. Barger, and J. E. Bunds, *Inorg. Chem.*, **7**, 1142 (1968).

f) Y. Fujii and M. Kodama, This Bulletin, **42**, 3172 (1969).

g) Calculated from the data for the CuA·PPS system.

---

[10] O. Yamauchi, Y. Nakao, and A. Nakahara, *ibid.*, **46**, 2119 (1973).

[11] R. C. Courtney, R. L. Gustafson, S. Chaberek, Jr., and A. E. Martell, *J. Amer. Chem. Soc.*, **81**, 519 (1959).

[12] J. W. Allison and R. J. Angelici, *Inorg. Chem.*, **10**, 2233 (1971).

[13] M. Tanaka, *J. Inorg. Nucl. Chem.*, in press.

As to the *p*-phenolsulfonate series, Cu(dpa) and Cu(terpy), both with aromatic nitrogens, form more stable mixed complexes than Cu(dien) does. The stabilities of the CuA·OH systems as seen from the log K_{OH} values exhibit the same trend as observed in the *p*-phenolsulfonate series.

The complexes with *n*-butylamine, CuA·BA, are more stable than CuA·PY and CuA·PPS, probably because of the high pK_a of *n*-butylamine. Their stabilities increase with added aromatic nitrogens and carboxylate oxygens.

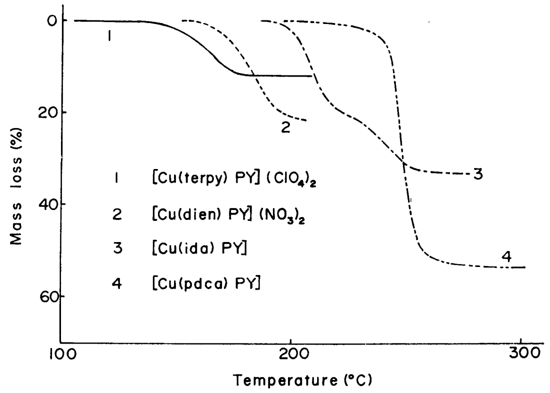


Fig. 4. Thermal analysis of CuA·PY.
Mass loss due to evaporation of pyridine:

Curve	Found (%)	Calcd (%)
1	12	14
2	21	21
3	31	29

Figure 4 shows the thermal decomposition curves of four pyridine-containing mixed complexes. Curves 1—3 correspond well to loss of pyridine from the complexes, and curve 4 may be explained in terms of decarboxylation of pyridine-2,6-dicarboxylic acid as well as evaporation of pyridine. The thermal stability is in the order Cu(terpy)·PY≤Cu(dien)·PY<Cu(ida)·PY<Cu(pdca)·PY, which is in line with the stability series in solution.

It is interesting to compare the stability of the copper(II)-pyridine bonding in CuA·PY with that in the binary complex according to the difference defined by the equation:

$$\Delta \log K_m = \log K_m - \log K_1$$

where $\log K_1 = 2.52$ (Ref. c) in Table 2) and refers to the stability constant of the 1:1 copper(II)-pyridine complex. The $\Delta \log K_m$ values are calculated to be negative for Cu(dien) (−0.75), Cu(dpa) (−0.76), Cu(terpy) (−0.71), and Cu(edma) (−0.43), and positive for Cu(ida) (0.13) and Cu(pdca) (0.45), which indicates that the bonding is destabilized in the first four complexes as compared with the binary complex.[14]

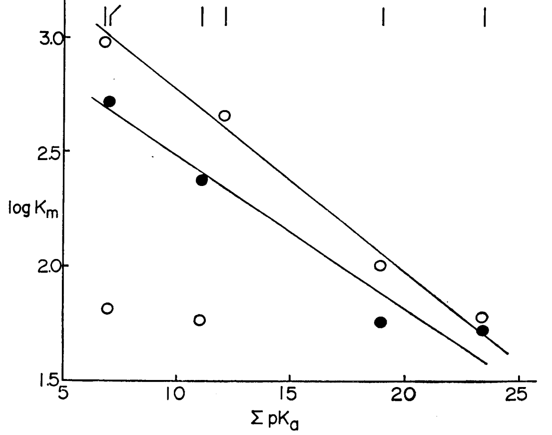


Fig. 5. Relationships between log K_m and $\sum$ pK_a in the CuA-PY and CuA·PPS series.
CuA·PY: ○, CuA·PPS: ●.

The affinity of the binary complex CuA for the second ligand L is considered to be dependent on the electronegativity of the central metal ion or, inversely, the basicity of the first ligand A. If A is a strong base, copper(II) in CuA will be less electrophilic and its binding with L will be weaker. Thus, we may expect a certain relationship between the stability constant log K_m and the sum of pK_a of the corresponding A, $\sum$pK_a, which is taken as indicative of the strength of the ligand as a Lewis base. From the plots of log K_m against $\sum$pK_a as shown in Fig. 5 for CuA·PY and CuA·PPS, we see a general trend in the four series that the stabilities of the ternary complexes usually decrease with the increase of the basicity of A with some anomalies. The exceptionally low stabilities of Cu(terpy)·PY and Cu(dpa)·PY are explained to be due to the steric interactions, as visualized by the molecular models, of 2,2′,2″-terpyridine or dipicolylamine with incoming pyridine, because the corresponding complexes with *p*-phenolsulfonate and hydroxy group are satisfactorily in the expected order. As pointed out by Sone *et al.*,[15] steric requirements for the second ligand can be a decisive factor leading to the stabilization in the mixed complex, and the above instances may be regarded as the results of the steric effects exerted on the part of the second ligand in a negative way.

On the other hand, a somewhat different view is also possible regarding the stability of mixed complexes. Griesser and Sigel[1] stressed the importance of back-donation in the formation of the ternary complexes which have π-acceptors such as 2,2′-bipyridine and pyrocatechol. They observed the favored formation of Cu(2,2′-bipyridine)·pyrocatechol, compared with Cu(2,2′-bipyridine)·ethylenediamine, and ascribed it to the cooperative interactions of the two π-acceptors.

---

[14] However, on purely statistical ground, we should take into account the factors due to preoccupation of the coordination sites in CuA. If we simply assume copper(II) to be four-coordinate, we may correct the K_1 value according to the equation

$$\frac{K_{n+1}}{K_n} = \frac{n(N-n)}{(n+1)(N-n+1)}$$

where N and n refer to the coordination number of copper(II) and the sites occupied by ligand as in $[\mathrm{Cu(H_2O)}_{N-n}\mathrm{L}_n]$, respectively. Since PY in CuA·PY is the fourth ligand to get into the site, we may take K_4/K_1 as the correction factor:

$$\frac{K_4}{K_1} = \frac{K_2}{K_1} \times \frac{K_3}{K_2} \times \frac{K_4}{K_3} = \frac{1}{16}.$$

This gives us the statistical value of 1.32 in place of 2.52 and makes all the Δ log K_m values positive.

[15] K. Sone, S. Utsuno, and T. Ogura, *J. Inorg. Nucl. Chem.*, **31**, 117 (1969).

In accordance with their finding, Cu(dpa)·PPS and Cu(terpy)·PPS are more stable than Cu(dien)·PPS and Cu(edma)·PPS.

An alternative explanation is based on Pearson's rule of hard and soft acids and bases,[1,16,17] according to which back-donation in CuA makes Cu(II) a harder acid which favors the bonding with hard bases like *p*-phenolsulfonate and hydroxy group. The stability sequences observed in the CuA·PPS and CuA·OH series serve as the evidence for this view. All these observations suggest that combination around copper(II) of aromatic nitrogens with negative oxygens is more favorable than that between nitrogen atoms only.

Considering that the stability of binary complexes is proportionally related to the pK_a of ligands, the mentioned effects of $\sum$pK_a suggest that the second ligand L has greater affinity for CuA having lower stability, provided that steric factors are negligible. This may point to the favorable combination, or the selectivity, of ligands around metal ions in general.

The authors are grateful to Mr. Yasuaki Uno of this college for measurement of thermal stability and to the members of the Osaka University Computation Center for computation. This investigation was supported in part by a grant from the Ministry of Education.

---

16) R. G. Pearson, *J. Amer. Chem. Soc.*, **85**, 3533 (1963).

17) S. Kida, *Kagaku no Ryoiki*, **24**, 541 (1970); This Bulletin, **34**, 962 (1961).