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Effects of Steric Factors on the Equilibrium and Thermodynamic Conditions of Mixed Ligand Complexes of the Copper(II) Ion with Diamines

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pH-Metric equilibrium investigations were carried out to determine the stability constants of sixteen copper(II)–diamine–glycine or copper(II)–diamine–diamine mixed ligand complexes. The corresponding enthalpy values were obtained in calorimetric measurements.

In every system studied, an increased stability was observed compared to the statistical case. It was found that, for a given "B" ligand, the formation of the mixed ligand complexes is the more favoured, the greater the difference between the $\log K_1/K_2$ *values of the parent complexes. The stability increase was explained by the larger enthalpy change in the copper(II)–diamine–diamine complexes, and by the combined effect of the enthalpy and entropy changes in the copper(II)–diamine–glycine systems.*

Introduction

During the past twenty years, increasing attention has been paid to the investigation of the factors influencing mixed ligand complex formation. The results achieved have been described in a number of reviews and books [1–9]. These works reveal that, as in the early stages of equilibrium chemistry [10], mixed ligand complexes containing diamines or polyamines have been, and still are, dealt with very extensively. In this respect, most data are available for systems involving the copper(II) ion.

More recent studies [11] relating to metal ion–polyamine parent complexes have shown that, in addition to species of the simple type MA_n, the formation of protonated and mixed hydroxo complexes must also be reckoned with frequently in equilibrium systems. Since we also arrived at a similar result in the investigation of the copper(II)–histamine system [12, 13], it appears necessary to re-examine the parent complexes too in a study of the mixed ligand complexes. This is all the more important if it is considered that although the equilibrium data are barely affected by the formation of protonated or mixed hydroxo complexes in low concentrations the enthalpy changes are influenced to a very large extent. As regards the factors affecting the formation of mixed ligand complexes [9] a number of conceptions are to be found in the more recent complex chemical literature [1–7, 9]. It may be stated from these that, besides the statistical factor, other constituents of fundamental importance in determining the stability are the steric, electrostatic and structural factors.

Up to the present there have been relatively few publications dealing with thermodynamic studies on mixed ligand complexes [12, 14]. However, it is important to carry out calorimetric measurements, as thermodynamic data differing from their statistical values may certainly originate from special effects arising in the course of mixed ligand complex formation.

In an earlier publication [12] we described studies relating to the copper(II)–histamine–aminoacid mixed complexes, where the increased stability was explained by a large entropy effect. However, it has emerged from more recent measurements [13] that other species too, in addition to the parent complexes, must be considered in the copper(II)–histamine system. In our earlier work this was not taken into account [12], and accordingly the enthalpy changes reported there for the mixed complex must be corrected.

As to the mixed complexes, in order to draw appropriate conclusions about their formation, the experiments must be extended to a large number of systems of similar type.

In accordance with the above, in the present work we report equilibrium and calorimetric results on the copper(II)–diamine–diamine and copper(II)–diamine–glycine mixed ligand complexes. The diamines examined were ethylenediamine (en), 1,3-diaminopropane (pn), N,N'-dimethylethylenediamine (sdmen), N,N-dimethylethylenediamine (admen), N,N,N',N'-tetramethylethylenediamine (tmen) and histamine (hm).

Experimental

Compounds Used and Experimental Conditions

The glycine and histamine used were Reanal products of p.a. quality, and the diamines were Fluka products of *puriss.* quality. The glycine and the histamine dihydrochloride were purified by double recrystallization from an ethanol–water mixture, and the diamines by vacuum distillation. Both the pH-metric and the calorimetric investigations were carried out at 25 °C, with an ionic strength of 0.2 mol/dm^3 KCl. Determination of the concentrations of stock solutions, and pH-metric [15] and calorimetric [13] measurements were performed as described previously.

Calculations

The species formed in the system examined can be described by the following general equilibrium equation:

$$pCu + qH + rA + sB \rightleftharpoons Cu_pH_qA_rB_s + \Delta H_{pqrs} \quad (1)$$

The corresponding stability constants are:

$$\beta_{pqrs} = \frac{[Cu_pH_qA_rB_s]}{[Cu]^p[H]^q[A]^r[B]^s} \quad (2)$$

(The signs of the charges are neglected in the equations).

The stability constants and enthalpy values were calculated from the pH-metric and calorimetric titration curves as reported earlier [16].

The equilibrium constants and enthalpy values listed in Tables IV and V in connection with the mixed ligand complexes can be defined by the following equation (q = 0):

$$Cu + A + B \rightleftharpoons CuAB + \Delta H_{111} \quad (3)$$

while the relevant stability constant is

$$\beta_{111} = \frac{[CuAB]}{[Cu]\,[A]\,[B]} \quad (4)$$

The stabilization constant $\Delta\log\beta_{111}$ arises from the difference between the measured values and those calculated from statistical considerations:

$$\Delta\log\beta_{111} = \log\beta_{111} - \frac{1}{2}(\log\beta_{120} + \log\beta_{102} + \log 4) \quad (5)$$

For the equilibrium

$$CuA_2 + CuB_2 \rightleftharpoons 2\,CuAB + \Delta H_M \quad (6)$$

the mixing constant K_M is given by

$$K_M = \frac{[CuAB]^2}{[CuA_2]\,[CuB_2]} \quad (7)$$

The value of $\Delta\log K$ expressing the ratio of the stepwise stability constants (corresponding to $\log K_1/K_2$ for the parent complexes) is obtained from the equations:

$$Cu + CuAB \rightleftharpoons CuA + CuB \quad (8)$$

$$K = \frac{[CuA]\,[CuB]}{[Cu]\,[CuAB]} \quad (9)$$

The equilibrium constants K_{AB} and K_{BA} relating to the coordination of the second ligand may be obtained from the following two equations:

$$CuA + B \rightleftharpoons CuAB + \Delta H_{AB} \quad (10)$$

$$CuB + A \rightleftharpoons CuAB + \Delta H_{BA} \quad (11)$$

Results and Discussion

Although the protonation constants of the ligands and the proton dissociation heats are well known from the literature, these values do not in general refer to the ionic strength of 0.2 mol/dm^3 KCl employed in the present work. Accordingly, the values were determined newly in the course of this work. The data are listed in Table I. The thermodynamic data relating to histamine and 1,3-diaminopropane [13] are given again here for comparison.

The error in the protonation constants in Table I is ± 0.02 log unit, and that in the protonation heats is ± 0.5 kjoule/mol. As regards the ethylenediamine derivatives, it may be stated that the presence of the substituents, mainly in the case of admen and tmen, decreases both the protonation constants and the enthalpy changes. With regard to the electron-donating property of the alkyl chain, the phenomenon can clearly be explained by spatial causes. This is supported by the data for 1,3-diaminopropane, where increase of the chain length results in the

TABLE I. Protonation Constants and Proton Dissociation Heats of the Ligands Examined; t = 25 °C, I = 0.2 mol/dm^3 KCl.

Ligand	pK_1	pK_2	ΔH_1^D	ΔH_2^D
			kjoule/mol	
gly	2.36	9.55	4.4	44.3
en	7.19	9.99	44.6	49.2
pn	8.84	10.53	50.7	53.4
admen	6.57	9.65	33.0	41.6
sdmen	7.12	10.05	38.1	42.6
tmen	6.06	9.29	27.5	31.6
hm	6.17	9.89	32.3	53.2

TABLE II. Stability Constants of Copper(II) Parent Complexes, t = 25 °C, I = 0.2 mol/dm^3 KCl.

Ligand	log β_{CuA}	log β_{CuA_2}	log K_1/K_2	log β_{CuA_2H}	log β_{CuAOH}	log $\beta_{Cu_2A_2(OH)_2}$
gly	8.07	14.84	1.30	–	–	–
en	10.57	19.68	1.46	–	–	–
pn	9.65	16.82	2.48	–	–	–
admen	9.24	16.20	2.28	–	–	–
sdmen	9.94	16.97	2.91	22.66	–	–
tmen	7.45	–	–	–	0.47	2.52
hm	9.58	16.06	3.10	21.79	1.2	7.00

opposite effect because of the greater separation of the N atoms.

Table II contains the stability constants of the copper(II) parent complexes of the ligands.

The data of Table II show that for those complexes where the difference of the stepwise stability constants is comparatively large (see log K_1/K_2 values), other equilibrium processes too must be reckoned with, in addition to parent complex formation. As pointed out by Paoletti *et al.* [17, 18], among these processes the hydrolysis of species of the type CuA^{2+} is of particular importance. As was reported in some detail in the previous paper [13] dealing with histamine complexes, the hydrolytic process becomes marked when the metal ion:ligand ratio is less than 1:2. If the ligand is present in excess then the formation of hydroxo complexes below pH ~7 may be neglected. An exception to this is the case of tmen, for which formation of the mixed hydroxo complexes is favoured so much in any metal ion: ligand ratio that the complex of the type CuA_2^{2+} is not formed at all.

It emerges further from the data of Table II that formation of the protonated complexes CuA_2H^{3+} must also be taken into consideration in the copper(II)–sdmen and copper(II)–histamine systems [13]. In the copper(II)–admen system, where log K_1/K_2 is substantially smaller than for the previous two ligands, for a ligand excess the equilibrium conditions can be described within the limits of error by assuming only the species CuA^{2+} and CuA_2^{2+}.

It may be stated from the data of Table II that substituents on the N atom decrease the values of the stability constants compared to ethylenediamine. This decrease becomes particularly pronounced in the log K_2 values, which results the increase of log K_1/K_2. In accordance with the above, the formation of complexes of the type CuA_2^{2+} containing substituted diamines and histamine is sterically hindered, and this leads to the formation of protonated complexes CuA_2H^{3+} or mixed hydroxo complexes.

Taking into account the equilibrium conditions it proved possible to calculate the thermodynamic data. The relevant enthalpy and entropy changes are in Table III.

Parallel measurements indicated that the error in the enthalpy values listed in Table III is within ± 1 kjoule/mol. In the case of ethylenediamine and its derivatives, our results are in good agreement with the latest data of Paoletti *et al.* [11] and also numerous other literature values [19].

The thermodynamic data in Table III otherwise show changes of a similar manner to those for the stability constants. Namely, the presence of substituents on the ligand decreases the enthalpy changes of both processes in the successive complex formation reaction; this decrease however becomes marked mainly for the reaction $CuA + A \rightleftharpoons CuA_2$. The decrease of the enthalpy changes is otherwise accompanied by a slight increase of the entropy changes. The role of the steric hindrance is especially striking in the copper(II) complex of histamine, where formation of the species CuA_2^{2+} is associated with an enthalpy change 13 kjoule/mol less than in the case of the complex CuA^{2+}.

Determination of the stability constants of the mixed ligand complexes was extended to sixteen systems of various compositions. The equilibrium constants are given in Table IV.

The data of Table IV permit us to draw the following conclusions:

(i) The stabilization constants of the mixed ligand complexes and the values of log K_M (for a given B ligand) are the larger, the greater the difference between the log K_1/K_2 values of the parent complexes. The stability constant of the copper(II)–en–gly mixed ligand complex exceeds the statistical value by only a slight extent, while at the same time the stability increase is very considerable in the copper(II)–sdmen–gly and copper(II)–hm–gly systems. This is illustrated in Fig. 1, where the percentage distributions of the complexes formed in the copper(II)–sdmen–gly system are shown as a function of the pH. It is clear from Fig. 1 that the mixed ligand complex is already present in maximum amount from pH ~ 5.4. In accordance with the high stability constant, the complex formation reactions take place at lower pH compared to the copper(II)–sdmen system. In the range examined, therefore, formation of the complex of the type CuA_2^{2+} is virtually negligible (its amount at pH = 6 is 0.8%).

TABLE III. Thermodynamic Data on the Copper(II) Parent Complexes, t = 25 °C, I = 0.2 mol/dm³ KCl.

Ligand	$-\Delta H_{CuA}$	$-\Delta H_{CuA_2}$	$-\Delta H_{CuA_2H}$	ΔS_{CuA}	ΔS_{CuA_2}	ΔS_{CuA_2H}
	kjoule/mol			joule/mol K		
gly	25.6	53.9	–	70	103	–
en	53.4	104.1	–	23	27	–
pn	49.5	95.5	–	19	2	–
admen	40.5	80.7	–	41	39	–
sdmen	46.6	85.6	112.0	34	38	58
hm	54.3	95.4	129.0	1	–13	–16

TABLE IV. Stability Constants of the Copper(II) Mixed Ligand Complexes. t = 25 °C, I = 0.2 mol/dm³ KCl.

Ligand A	Ligand B	$\log \beta_{111}$	$\Delta\log \beta_{111}$	$\log K_M$	$\Delta\log K$	$\log K_{AB}$	$\log K_{BA}$
en	gly	17.69	0.13	0.86	0.95	7.12	9.62
pn	gly	16.91	0.78	2.16	0.81	7.26	8.84
admen	gly	16.70	0.88	2.36	0.61	7.46	8.63
tmen	gly	17.29	1.08	2.76	0.72	7.35	9.22
tmen	gly	15.22	–	–	0.30	7.77	7.15
hm	gly	17.00	1.25	3.10	0.65	7.42	8.93
pn	en	18.83	0.28	1.16	1.39	9.18	8.26
admen	en	18.55	0.31	1.22	1.29	9.31	7.98
sdmen	en	19.27	0.64	1.88	1.24	9.33	8.70
tmen	en	16.47	–	–	1.55	9.02	5.90
hm	en	18.66	0.49	1.58	1.49	9.08	8.09
admen	pn	16.98	0.17	0.94	1.91	7.74	7.33
sdmen	pn	17.51	0.31	1.22	2.08	7.57	7.86
tmen	pn	14.76	–	–	2.34	7.31	5.11
hm	pn	17.00	0.26	1.12	2.23	7.42	7.35
hm	sdmen	16.90	0.08	0.76	2.62	7.32	6.96

The observations relating to the role of $\log K_1/K_2$ is supported by our earlier data on copper(II)–amino-acid–amino/acid systems [20]. Stability constants differing from the statistical case were obtained only for mixed ligand complexes containing both aliphatic (*e.g.* alanine) and aromatic (*e.g.* tyrosine) amino-acids, where there is also a slight difference between the $\log K_1/K_2$ values.

(ii) In spite of the $\log K_1/K_2$ values for the copper (II)–glycine and copper(II)–ethylenediamine complexes being nearly the same, the stability increase is considerably higher in the copper(II)–diamine–gly systems than in the corresponding copper(II)–diamine–en complexes [21]. This phenomenon will be explained later. In the copper(II)–diamine–pn mixed complexes, where the value of $\log K_1/K_2$ is relatively large with the "B" ligand too, the increase in stability is only slight. This is particularly the case for the copper(II)–hm–sdmen system, where $\log K_1/K_2$ is large for both parent complexes, and thus $\Delta\log \beta_{111}$ has a very low value.

(iii) As pointed out earlier by Martin and Prados [9], conclusions drawn on the favoured stability of the mixed ligand complexes purely on the basis of the $\Delta\log \beta_{111}$ and $\log K_M$ values may be misleading. The differing stability conditions of the parent complexes may result in an effect whereby extensive mixed ligand complex formation occurs, without there being an acceptable reason for this. It is much more advantageous, therefore, to compare the stability conditions on the basis of the $\Delta\log K$ or $\log K_{AB}$ and $\log K_{BA}$ values. In a recent review Sigel [7] demonstrated that the statistical value of $\Delta\log K$ can be calculated in the knowledge of the geometry of the parent complex. In copper(II) complexes with distorted octahedral structures, if both ligands are bound to the metal ion by two donor atoms, then $\Delta\log K_{stat} = 0.9$. It follows from this that if $\Delta\log K_{measd.} < 0.9$, then mixed ligand complex formation is favoured in any case.

It may be stated from Table IV that in the copper (II)–diamine–en and copper(II)–diamine–pn mixed ligand complexes the value of $\Delta\log K$ varies in the range 1.24–1.55 and 1.91–2.34, respectively, which are in good agreement with the values of $\log K_1/K_2$ for copper(II)–en and copper(II)–pn: 1.46 and 2.48, respectively. This means that the ligands ethylenediamine and 1,3-diaminopropane may coordinate with almost the same probability to CuA^{2+} complexes formed by any type of diamine investigated. However, the measured $\Delta\log K$ values are substantially higher than the value of 0.9 for the

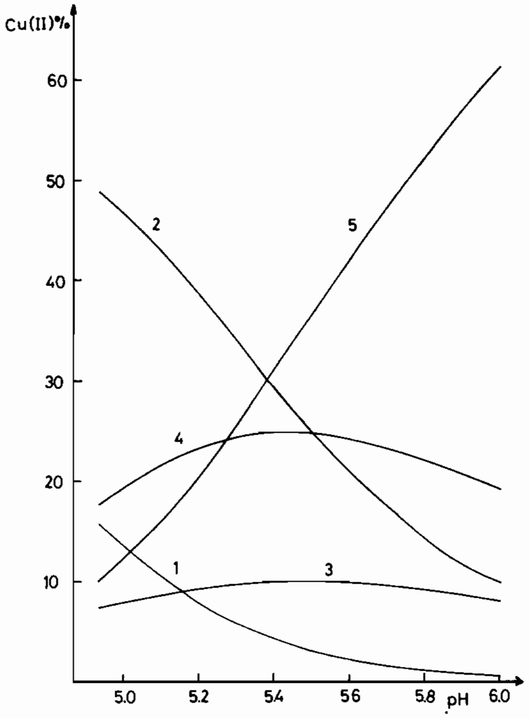

Fig. 1. pH-Dependent percentage concentration distribution of the species formed in the copper(II)–sdmen–gly system. 1, Cu^{2+}, 2, $Cu(gly)^+$; 3, $Cu(gly)_2$; 4, $Cu(sdmen)^{2+}$; 5, $Cu(sdmen)(gly)^+$. Initial concentrations: $[Cu^{2+}] = 5 \times 10^{-3}$, $[gly] = 5 \times 10^{-3}$, $[sdmen] = 5.1 \times 10^{-3}$ mol/dm³.

statistical case. On this basis it may be concluded that a certain degree of steric hindrance must also be taken into account in the mixed complexes. The extent of this, however, is much less than the effect in the case of one of the parent complexes, and this leads to considerable mixed ligand complex formation, which is reflected in the log K_M and $\Delta\log\beta_{111}$ values.

(iv) The situation is different to a certain extent in the copper(II)–diamine–glycine mixed ligand complexes. The value of Δlog K lies in the interval 0.30–0.95, and thus, with the exception of the copper(II)–en–gly system, the data indicate a stability increase in excess of the statistical effects. Accordingly, the favoured stability of the mixed ligand complexes of glycine cannot be explained only by the steric causes expressed in the stability conditions of the parent complexes. In the interpretation of this, attention must also be paid to the log K_{AB} values, which vary between 7.12 and 7.77. This is higher than the value of log $K_2 = 6.77$ for the copper(II)–glycine system, but lower than the stability constant log $K_1 = 8.07$ for the copper(II)–glycine complex of type CuA^+. The glycinate anion entering as second ligand therefore coordinates with higher stability to diamine complexes of type CuA^{2+} than to the corresponding glycine complex.

Coordination of glycine to the free copper(II) ion is also more favoured compared to copper(II)–diamine complexes of the type CuA^{2+}, which similarly have a positive charge of two. This phenomenon may be ascribed to the role of the change in charge, which is supported by the thermodynamic data in Table V.

From the differences between parallel measurements and between the enthalpy values calculated from the individual measurement points, the error in the data in Table V is within ± 2 kjoule/mol. When this is taken into account, it may be stated that the process shown in equation (6) is accompanied by an exothermic heat effect. In the event of a given "B" ligand, the value of ΔH_M to a good approximation increases in parallel with the mixing constant log K_M. It further appears that the value of ΔH_M is generally more negative in the copper(II)–diamine–en systems than in the corresponding copper(II)–diamine–glycine complexes. The difference between

TABLE V. Thermodynamic Data on Mixed Ligand Complexes of the Copper(II) Ion, t = 25 °C, I = 0.2 mol/dm³ KCl.

Ligand A	Ligand B	$-\Delta H_{111}$	$-\Delta H_M$	$-\Delta H_{AB}$	$-\Delta H_{BA}$	ΔS_{111}	ΔS_M
		kjoule/mol				joule/mol K	
en	gly	79.5	1.0	26.1	53.9	72	13
pn	gly	77.0	4.6	27.5	51.4	65	26
admen	gly	70.7	6.8	30.2	45.1	82	22
sdmen	gly	74.9	10.2	28.3	49.3	80	19
hm	gly	80.8	12.2	26.5	55.2	54	18
pn	en	102.9	6.2	53.4	49.5	15	1
admen	en	98.7	12.6	58.2	45.3	24	−19
sdmen	en	101.3	12.8	54.7	47.9	29	−7
hm	en	104.6	9.6	50.3	51.2	6	−2
admen	pn	90.4	4.6	50.1	40.9	22	3
sdmen	pn	94.1	7.0	47.5	44.6	19	0
hm	sdmen	91.6	2.2	37.3	45.0	16	7

the thermodynamic data of the former systems is particularly striking in the relevant entropy changes. In mixed ligand complexes containing glycine, ΔS_M has a fairly high positive value, whereas in the case of ethylenediamine or 1,3-diaminopropane as the "B" ligand the entropy change is nearly zero, and even negative in some cases. In connection with the interpretation of the entropy changes, it must also be taken into account that the value of ΔS_M is not zero even in the statistical case ($\Delta S_M^{stat} \sim 12$ joule/mol K).

In accordance with the above, the stability increase in the copper(II)–diamine–diamine mixed ligand complexes is reflected in the increased enthalpy change, which is accompanied by a slightly favoured entropy change. At the same time, in the copper(II)–diamine–glycine systems both the ΔH and the ΔS values assist the shift of reaction (6) in the direction of the upper arrow, which is indicative of the combined role of a change in charge and the absence of steric hindrance.

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