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Complexation Reactions of Copper(II) Ions with 16-Membered and 18-Membered Monocyclic Dioxopolyamines in an Aqueous Solution

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Synopsis. The equilibria of complexation reactions of dioxo[16]aneN$_5$, dioxo[18]aneN$_6$, and their related compounds with copper(II) ions were determined potentiometrically. Making a sharp contrast to the 13—15-membered monocyclic dioxotetramine system, they interact with copper(II) ions in their neutral and doubly deprotonated forms, L and $H_{-2}L^{2-}$, yielding stable CuL^{2+} and $CuH_{-2}L^0$ complexes.

In earlier studies on the complexation of 13—15-membered monocyclic dioxotetramines,[1,2] it was demonstrated that these potential quadridentate macrocycles only form square planar N$_4$ complexes, $MH_{-2}L^0$, with Cu(II) and Ni(II) ions as a result of a double deprotonation of the amides. The binding of the metal(II) is assumed to take place first at the amide group, followed by imidiate amide deprotonation and coordination. The latter coorperative action might occur more readily in the macrocycles than in the linear tripeptides, particularly in those having rigid planarity and suitable cavity sizes for the small metal ions having a stronger tendency to square-planar coordination like Cu(II) and Ni(II) ions.

As a continuation of our equilibrium study concerning the complexation reactions of macrocyclic dioxopolyamines, we have now determined the equilibria of copper(II) complex formations of dioxo[16]aneN$_5$, dioxo[18]aneN$_6$, and their related compounds. Comparisons of the present findings with those for the 13—15-membered macrocyclic dioxotetramines and the relevant linear tripeptides might shed more light on the ligating properties of macromonocyclic dioxopolyamines, leading to an explanation of their useful applications.

Experimental

The macrocyclic dioxopolyamines used were prepared according to methods described in the literature[1–4] (Chart 1). The salt $CuSO_4 \cdot 5H_2O$ was an analytical grade chemical and its solutions were standardized by EDTA titration.[5]

The pH-metric titrations were performed with a Mettler automatic titrator[6,7] under a nitrogen or an argon atmosphere at 25±0.2 °C. All of the experimental conditions and procedures employed have been mentioned previously.[6] The values of $-\log[H^+]$ were estimated by applying a correction of −0.13 pH unit to the pH readings.[7] The mixed protonation constants (K_i's) were determined potentiometrically.[4] The mixed protonation constants ($\log K_i$'s) of a new ligand, L^7, were 8.35, 4.85, and ca. 2.6 and those of L^9, 8.73 and 6.22.

Results and Discussion

The equimolar mixture solution of copper(II) and L^4, L^5, L^6, or L^9 in its fully protonated form (H_2L^{2+}) gave titration curves with a buffer region at the titration point $4>a>0$, which fitted to the theoretical equation (16) in Ref. 1 derived for the formation of $CuH_{-2}L^0$ in the dioxotetramine system ($C_M=C_L$). Therefore, the cumulative formation constants, $K_{CuH_{-2}L}(=[CuH_{-2}L^0]\cdot[H^+]^2/[Cu^{2+}]\cdot[L])$, were determined similarly in a graphic way.[1]

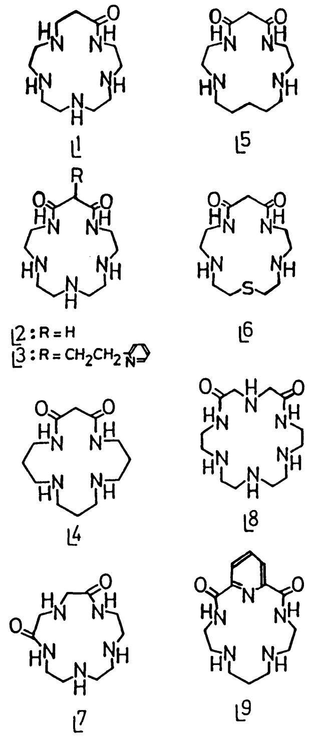

Chart 1.

In sharp contrast with these ligand systems, the titration curve of an equimolar mixture of Cu(II) and L^2 (dioxo[16]aneN$_5$) in its fully protonated form (H_3L^{3+}) gave two buffer regions at titration points $3>a>0$ and $5>a>3$ (Fig. 1). Two breaks, one occurring at $a=3$ and the other at $a=5$ suggest the complexation equilibria (1) and (2) for the titration points $3>a>0$ and $5>a>3$, respectively. The K_{CuL} value was determined in an analogous way to that described for the complexation of the macromonocyclic triamine with copper(II) ions.[8] The K^{-2H} value was then estimated from the gradient of the straight line between

$$Cu^{2+}+L=CuL^{2+},\ K_{CuL}=[CuL^{2+}]/[Cu^{2+}]\cdot[L] \tag{1}$$

$$CuL^{2+}=CuH_{-2}L^0+2H^+,\quad K^{-2H}=[CuH_{-2}L^0]\cdot[H^+]^2/[CuL^{2+}] \tag{2}$$

the $(\alpha'/2)/(C_L-\alpha'/2)$ and $[H^+]^{-2}$ (Fig. 2). Here, α' is

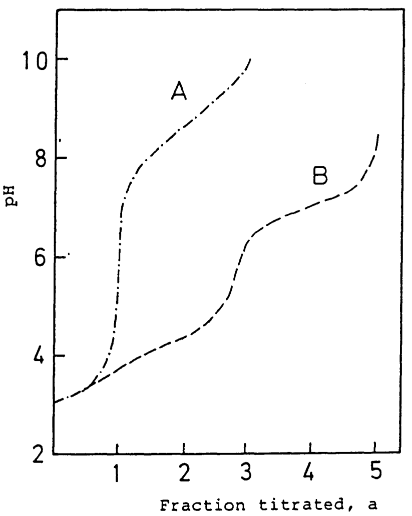

Fig. 1. Titration curves of 1.00 mM dioxo[16]aneN$_5$ (3HCl salt).
Ionic strength (I)=0.20 M, 25 °C, (A) dioxo[16]aneN$_5$ only, (b) dioxo[16]aneN$_5$+1.00 mM Cu(II), sample solution 50.0 ml with 0.100$_0$ M tetraethylammonium solution.

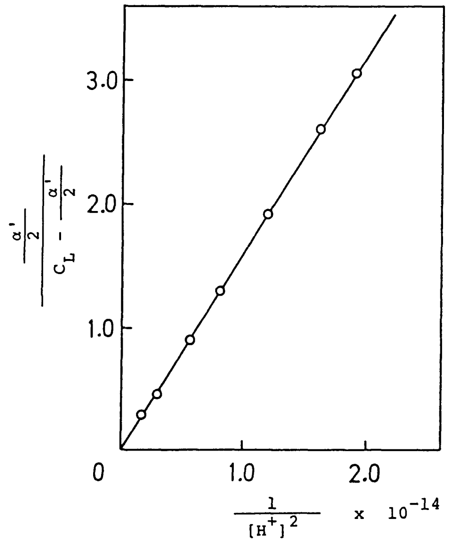

Fig. 2. Plots of $(\alpha'/2)/(C_L-\alpha'/2)$ against $1/[H^+]^2$.
[Cu(II)]=1.00 mM, [dioxo[16]aneN$_5$ 3HCl]=1.00, mM, I=0.20 M, 25 °C.

defined as $(a-3)C_L+[H^+]$, and $(\alpha'/2)/(C_L-\alpha'/2)$ corresponds to the $[CuH_{-2}L^0]/[CuL^{2+}]$ ratio. This also turned out to be the case for the 1 : 1 Cu(II)-dioxo[18]aneN$_6$(L^8) mixture solution ($4>a>0$, $6>a>4$). The K_{CuL} and K^{-2H} values for the Cu(II) complex of dioxo[18]aneN$_6$ were also estimated in a quite similar way.

In the case of a Cu(II)-monooxo[16]aneN$_5$(L^1, H_4L^{4+}) system, two breaks occurring at a=3 and 5 suggest the formation of $CuHL^{3+}$ and $CuH_{-1}L^+$. The K_{CuHL} $(=[CuHL^{3+}]/[Cu^{2+}]\cdot[HL^+]$ value was determined by using the following equation (3) derived in an identical manner as that employed for the complexation of macromonocyclic pentamines with Zn(II) ions ($C_M=C_L$).[8)]

$$\frac{K_{CuHL}\cdot[H^+]}{K_4}(3C_L-\alpha)^2(\alpha_H)_L = (\alpha(\alpha_H)_L-\beta_H C_L)\cdot(3(\alpha_H)_L-\beta_H). \qquad (3)$$

Here, K_4 means the 4-th dissociation constant of H_4L^{4+}. As in the case of the dioxo[16]aneN$_5$ system, the K^{-2H} $(=[CuH_{-1}L^+]\cdot[H^+]^2/[CuHL^{3+}])$ value was determined from the gradient of the straight line between the $(\alpha'/2)/(C_L-\alpha'/2)$ $(=[CuH_{-1}L^+]/[CuHL^{3+}])$ value and $[H^+]^{-2}$. The titration of an equimolar mixture of Cu(II) and dioxo[15]aneN$_5$ (L^7, H_3L^{3+}) also gave two breaks at a=4 and 5, suggesting the formation of $CuH_{-1}L^+$ and $CuH_{-2}L^0$. The $K_{CuH_{-1}L}$ $(=[CuH_{-1}L^+]\cdot[H^+]/[Cu^{2+}]\cdot[L])$ and $K^{-H}_{CuH_{-1}L}$ $(=[CuH_{-2}L^0]\cdot[H^+]/[CuH_{-1}L^+])$ values for the Cu(II)-L^7 complex were determined in an identical manner as that previously applied to the Cu(II)-dioxo[12]aneN$_4$ complex formation.[2)] All of the equilibrium constants determined in this study are listed in Table 1.

The equimolar mixture solution of Cu(II) ion and dioxo[16]aneN$_5$ at pH 4—5 (at titration point $a<3$) is blue, greatly differing from the pink (λ_{max}=505 nm) shown by the square-planar Cu(II)-dioxo[14]aneN$_4$ complex $CuH_{-2}L^0$,[2,9)] However, it turns to violet at pH's higher than 7.0, indicating a certain change in the coordination mode of dioxo[16]aneN$_5$ to the Cu(II) ion. In light of the similarity between the visible spectra of the blue complex and $[Cu(dien)(OH_2)_3]^{2+}$ (λ_{max} for the blue complex is 610 nm and that for the $[Cu(dien)(OH_2)_3]^{2+}$ complex is 611 nm[10)]), the tetragonally distorted octahedral structure, where the three amino nitrogen donors and one H$_2$O stay at

Table 1. Equilibrium Constants of Copper(II) Complexes.
Ionic Strength (I)=0.20, 25 °C

Ligand	K_{CuHL}	K_{CuL}	$K_{CuH_{-1}L}$	$K_{CuH_{-2}L}$	K^{-2H}
Monooxo[16]aneN$_5$(L^1)	$(1.1\pm0.1)\times10^7$	—	$(2.8\pm0.5)\times10^3$	—	$(2.5\pm0.2)\times10^{-4}$
Dioxo[16]aneN$_5$(L^2)	—	$(9.8\pm1.0)\times10^{11}$	—	$(1.6\pm0.5)\times10^{-2}$	$(1.6\pm0.3)\times10^{-14}$
Pyr-dioxo[16]aneN$_5$(L^3)	—	$(1.1\pm0.1)\times10^{14}$	—	$(2.6\pm0.7)\times10^{-2}$	$(2.5\pm0.4)\times10^{-16}$
Dioxo[16]aneN$_4$(3,3,3,3)(L^4)	—	—	—	$(4.4\pm0.6)\times10^{-11}$	—
Dioxo[16]aneN$_4$(3,2,5,2)(L^5)	—	—	—	$(1.3\pm0.2)\times10^{-5}$	—
Dioxo[16]aneN$_4$S(L^6)	—	—	—	$(1.5\pm0.2)\times10^{-3}$	—
Dioxo[15]aneN$_5$(L^7)	—	—	$(7.3\pm0.8)\times10^2$	$(3.0\pm0.8)\times10^{-6}$	$(4.1\pm0.6)\times10^{-9}$[a)]
Dioxo[18]aneN$_6$(L^8)	—	$(3.6\pm0.5)\times10^{10}$	—	$(9.4\pm1.5)\times10^{-6}$	$(2.6\pm0.4)\times10^{-16}$
Dioxopyo[16]aneN$_5$(L^9)	—	—	—	$(1.4\pm0.2)\times10^{-2}$	—

a) $K^{-H}_{CuH_{-1}L}$.

the basal positions, would be assumed for the blue complex. In fact, a Dreiding molecular model study shows that the Cu(II) ion in this complex can have a coordination environment of three amino nitrogen donors and one carbonyl oxygen of L^2 in plan with two H_2O molecules above and below, completing the distorted octahedral coordination. The formation constant, K_{CuL}, determined in this study is slightly larger than that of the copper(II)-diethylenetriamine (dien) complex ($\log K_{CuL}=10.01$).11) This finding also lends a strong support to the above explanation.

As in the case of the nickel(II)-dioxo[16]aneN_5 complex, $NiH_{-2}L^0$,4) the doubly-deprotonated dioxo-[16]aneN_5 anion for the violet complex, $CuH_{-2}L^0$, which is formed at pH's higher than 7.0, would encircle the Cu(II) ion in a square-pyramidal configuration with two deprotonated amide nitrogen donors staying at the basal positions, along with the two amino nitrogens, probably completing the distorted octahedral coordination. The 16-membered dioxotetramine, dioxo[16]aneN_4 (3,3,3,3)(L^4), forms solely $CuH_{-2}L^0$. Its violet aqueous solution displays visible spectra ($\lambda_{max}=550$ nm) similar to those for the dioxo[16]aneN_5 complex, $CuH_{-2}L^0$. Hence, for this complex the distorted octahedral coordination including water molecules must be likely. A molecular model examination shows that the ligand in this complex can encircle the Cu(II) ion with two amino and two deprotonated amide nitrogens staying at the basal positions with two H_2O molecules at the axial coordination sites. The other 16-membered dioxotetramine, L^5, also afforded the $CuH_{-2}L^0$ complex. Its aqueous solution, however, is pink and gives visible spectra quite similar to those of Cu(II)-13—15-membered dioxotetramine complexes.2,4) This implys that the structure of the Cu(II)-L^5 complex can be described as an extremely flattened tetrahedron or a square-planar geometry.12) L^9 and L^6 also yielded only stable $CuH_{-2}L^0$ under the present experimental conditions. The significant difference in the magnitude of $K_{CuH_{-2}L}$ value between L^4 and L^5 complexes clearly suggests that the presence of the dioxo-[2.3.2]tetramine moiety is essentially required for the formation of stable doubly-deprotonated $CuH_{-2}L^0$ (Table 1), because the doubly-deprotonated dioxo-[2.3.2]tetramine frame can adapt most easily to the achievement of the rigid square-planar geometry.

As demonstrated by the $K_{CuH_{-2}L}$ values in Table 1, the sulfur and pyridine nitrogen donors incorporated within the 16-membered macrocyclic frame also assist in stabilizing the complex. Dioxo[18]aneN_6, L^8, also forms blue CuL^{2+} at pH 3.5—6.0, and mauve doubly-deprotonated $CuH_{-2}L^0$ at pH's higher than 7.5. The fact that dioxo[16]aneN_5 and dioxo[18]aneN_6 can form CuL^{2+} as well as $CuH_{-2}L^0$, but L^5 gives only $CuH_{-2}L^0$ clearly suggests that neutral dioxopolyamines can encircle the copper(II) ion in their macrocyclic cavity only when three or more amine nitrogens are available for the complexation.

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