CHEMISTRY LETTERS, pp. 109-112, 1994.

Ligand Exchange of Cu(II)-Polyaminopolycarboxylate with Penicillamine. Evaluation of the Stability of Metal Complexes in Dynamic Aspects

Akira HANAKI* and Hiromitsu SAGO†
Faculty of Engineering, Shizuoka University, Hamamatsu 432

Stopped-flow kinetic studies have been done on the ligand-exchange of Cu(II) complexes of polyaminopolycarboxylate (EDMA, EDDA, EDDP, EDTA and EDTPO) with penicillamine to yield Cu(II)-bis(penicillamine). The reaction consists of two steps and the transient which is a ternary complex has been characterized. A fairly good correlation existed between the stability constants of the mother complexes and the rate constants of ligand-exchange.

The stability of metal complexes has been defined by the term "Stability Constant ", which is expressed by the ratio of the rates of formation to dissociation of the complex.[1-3] The stability constant thus defined could not imply as to whether the complex is labile, i.e.under rapid equilibrium, or inert, i.e., under slow equiliblium. In order to elucidate a function of the complex, for example transport of the metal ion from a ligand to another, dynamism of the metal ion-ligand interaction is an important concept. We would estimate the stability of metal complexes in dynamic aspects. The metal ion discussed here is Cu(II). The Cu(II)-ligand interaction given in equation (1) is generally under rapid equilibrium. If the equilibrium is perturbed by addition of another ligand(L'), it would be scrambled undergoing chemical relaxation to shift towards new equilibrium states as

$$\mathrm{Cu(II)} + \mathrm{L} \rightleftharpoons \mathrm{Cu(II)L} \qquad (1)$$

$$\mathrm{Cu(II)L} + \mathrm{L'} \rightleftharpoons \mathrm{L'Cu(II)L} \qquad (2)$$

$$\mathrm{L'Cu(II)L} + \mathrm{L'} \rightleftharpoons \mathrm{Cu(II)L'_2} + \mathrm{L} \qquad (3)$$

---

† Present address: Division of Informatics for Sciences, Graduate School of Human Informatics, Nagoya University, Nagoya 464-01.

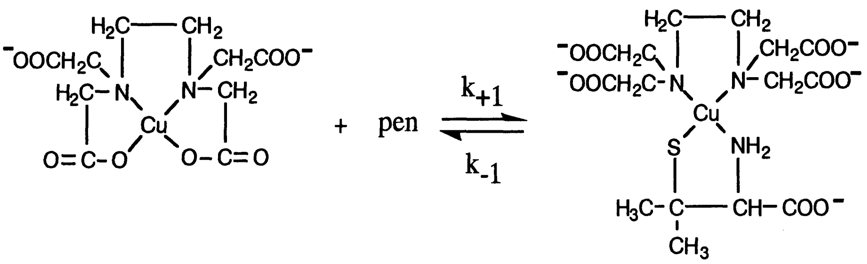
shown in equations (1), (2) and (3). The relaxation time, which is related to the rate of ligand-exchange, would depend on the stability of Cu(II)L and/or Cu(II)L'$_2$.$^{4)}$

When the complexes L'Cu(II)L and Cu(II)L'$_2$ possess characteristic spectroscopic properties different from the mother complex Cu(II)L, the rate of ligand-exchange can be determined easily and accurately.$^{5)}$ And, if those complexes could be characterized, the reaction mechanism for the ligand-exchange is elucidated on a molecular basis. For those purposes, the reaction of Cu(II) and penicillamine is a suitable system. At first, the Cu(II) complexes containing penicillamine(pen) display S→Cu(II) charge transfer(LMCT) band at 330-360 nm.$^{6)}$ Secondly, the complexes are relatively stable as compared with those from cycteine or 2-mercaptoethylamine, and do not undergo oxido-reduction during the ligand-exchange reactions. In this communication, the ligand-exchange reactions of Cu(II)-ethylenediaminetetraacetate(EDTA) and its related compounds with pen were described to estimate the stability on dynamic basis.

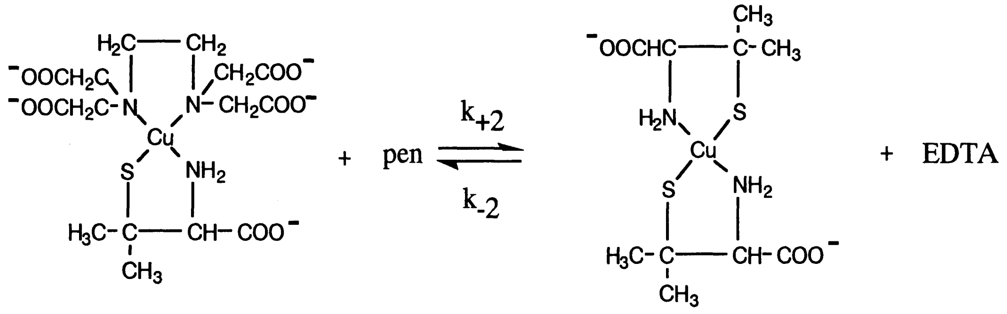
Ligands used were ethylenediamine-N-acetic acid(EDMA),$^{7)}$ ethylenediamine-N,N'-diacetic acid(EDDA), ethylenediamine-N,N'-dipropionic acid(EDDP), EDTA and ethylenediamine-N,N,N',N'-tetrakis (methylenephosphonic acid)(EDTPO).$^{8)}$ Those are the compounds having ethylenediamine-skelton with different numbers of acetate group as a pendant ligand, or with different kinds of pendants. The rates were all determined by a stopped-flow technique. The mother complex, Cu(II)-polyaminopolycarboxylate, undergoes ligand-exchange by pen yielding Cu(II)-(pen)$_2$. In order to detect and characterize transients which might be formed in the course of the ligand-exchange reaction, the absorption spectra were measured in the 280-450 nm region by the stopped-flow and point-by-point method.$^{9)}$ An apparent rate for the ligand-exchange under pseudo frist-order conditions using a large excess of pen were obtained from the absorbance-time plot at λ_{max} of LMCT band. Plot of the observed rate constant k_{obsd} against [pen] gave a straight line indicating the reaction to be first-order to both the mother complexes and pen. The foward rate constant (k_+) and backward constant (k_-) for the ligand-exchange were determined from the slope and the intercept, respectively.$^{10)}$ Both the spectral and kinetic measurements were done mainly in I=0.1 M(NaClO$_4$) at 25 ℃ and pH 9.2 (1 M=1 mol dm^{-3}).

The absorption spectrum of the transient obtained at the initial stage of the Cu(II)-EDTA and pen reaction showed λ_{max} at 355 nm, while the final product Cu(II)-(pen)$_2$ showed two absorption bands at λ_{max} = 330 and 385 nm. Chemical composition and formation constant, K_f, of the transient were determined by the stopped-flow and molar-ratio method.$^{9)}$ The ratio of [EDTA] / [Cu(II)] / [pen] was determined to be 1/1/1, indicating the formation of a ternary complex having the following parameters ($\varepsilon = 4.8 \times 10^3$ M^{-1}cm^{-1} and $K_f = 5.93 \times 10^3$ M^{-1}). Those findings indicate that the ligand-exchange reaction between Cu(II)-EDTA and pen to yield Cu(II)-

$(pen)_2$ is described by equations (A) and (B). The rate of formation of the ternary complex was extremely rapid at pH 9.2 so that the rate constant k_{+1} could not be determined at 25 ℃; the k_{+1} at 5 ℃ was $1.3 \times 10^5\ M^{-1}s^{-1}$.



(A)



(B)

Formation of the ternary complexes from the Cu(II) complexes of polyaminopolycarboxylate with acetate or propionate groups was extremely rapid. Though the rate constants could not be determined accurately, the reactivity in decreasing order was as follows; Cu(II)EDMA > Cu(II)EDDP > Cu(II)EDDA > Cu(II)EDTA. On the contrary, the reaction of Cu(II)EDTPO and pen appeared to be relatively slow as compared with other complexes. Then, detection of the ternary complex did not succeed, because k_{+1} would be smoller than k_{+2}. Spectral parameters for the ternary complexes at pH 9.2 and 25 ℃ are as follows: $\lambda_{max}/nm(\varepsilon_{max}/M^{-1}cm^{-1})$; (EDDP)-Cu(II)-(pen); 345 (4670), (EDDA)-Cu(II)-(pen); 345 (4390), (EDTA)-Cu(II)-(pen); 357 (4430).[11)]

The rate constant k_{+2} was at least three orders of magnitude less than k_{+1}, and the constants of the reverse reactions, k_{-1} and k_{-2}, were at least two orders of magnitude less than the corresponding constants of the forward reactions. Then, the dynamic equilibrium constant, expressed by $K_1=k_{+1}/k_{-1}$ and $K_2=k_{+2}/k_{-2}$, would be aproximately $\sim 10^2\ M^{-1}$ or larger. Plot of the stability constants K of the mother conplexes against k_{+2} are summarized in Fig.1. The complexes with same kind but different numbers of the pendant appeared to have a fairly good correlation between K and k_{+2}. In other words, as numbers of the pendant increased, the mother complex was stabilized and the ternary complex likewise became inert. Both the Cu(II) complexes of EDDA and EDDP complexes having similar stability constants showed different lability; the ternary complex with EDDP appeared to undergo more rapid ligand-exchnge than that with EDDA. Of much interest is that the complex having EDTPO barely undergoes ligand exchange. The pendant which would not be coordinated directly to the Cu(II) ion in the ternary complex affects the lability of the complex. A detailed account on the dynamic equilibrium and the participation of the pendant in the ligand-exchange will be published elsewhere.

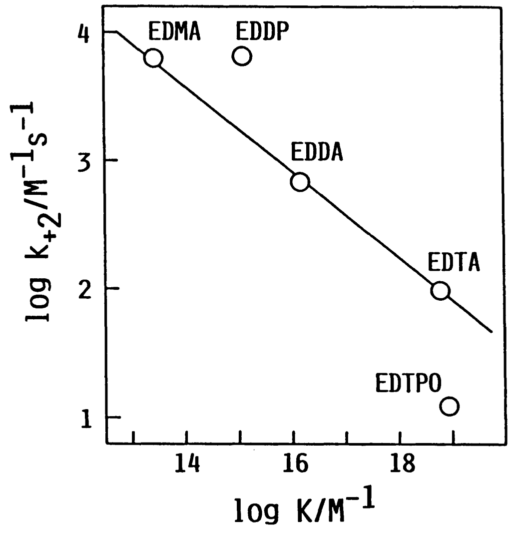


Fig.1. Rate constant-stability constant relationship.

References

1) J. Bjerrum, "Metal Ammine Formation in Aqueous Solution, " Haase, Copenhagen (1941).

2) F. J. C. Rossotti and H.Rossotti, "The Determination of Stability Constants, " McGraw-Hill, New York (1961).

3) "Stability Constants of Metal-ion Complexes, " ed by L. G. Sillen and A. E. Martell, The Chemical Society, London (1964), Supplement No. 1 (1971).

4) D. W. Margerum, G. R. Cayley, D. C. Weatherburn, and G. K. Pagenkopf, "Coordination Chemistry, " ed by A. E. Martell, ACS Monograph 174, (1978) Vol. 2, pp 1-220, and references therein.

5) A. Hanaki, *Chem. Pharm. Bull.*, **22**, 2491 (1974).

6) A. Hanaki, *Chem. Lett.*, **1980**, 626; *ibid.*, **1981**, 139 .

7) H. Masuda, A. Odani, T. Yamazaki, T. Yajima, and O. Yamauchi, *Inorg. Chem.*, **32**, 1111 (1993).

8) E. N. Rizkalla and M. T. M. Zaki, *Talanta*, **27**, 769 (1980).

9) A. Hanaki H and Yokoi, *Chem. Lett.*, **1991**, 1311.

10) N. Yoshida and M. Fujimoto, *Chem. Lett.*, **1980**, 231.

11) λ max/nm (ε max/$M^{-1}cm^{-1}$) for (EDMA)-Cu(II)-(cysteine); 338 (3780), (EDDA)-Cu(II)-(cysteine); 344 (4380), A. Hanaki, unpublished data.

(Received September 9, 1993)