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Contribution from the Department of Chemistry, College of General Education, Hirosaki University, Bunkyo, Hirosaki 036, Japan, the Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi, Hiroshima 734, Japan

Displacement Kinetics of Copper(II) Macrocyclic Triamines with EDTA and CyDTA

MUTSUO KODAMA,[1a] TAKASHI YATSUNAMI,[1b] and EIICHI KIMURA*[1b]

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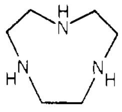
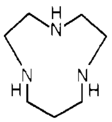
Ligand–ligand replacement kinetics have been measured for the reaction of Z (=EDTA or CyDTA) with 1:1 copper(II) complexes of the macrocyclic triamines 9-membered 1,4,7-triazacyclononane (L^1) and 10-membered 1,4,7-triazacyclodecane (L^2) in ammonia buffer solutions. The results are compared with the previously reported rate data for the same exchange reaction of linear dien (L^3) complex to see effects of the ligand cyclization and of the ring size. The common rate law is $d[CuZ^{2-}]/dt = k_Z[CuL^{2+}][Z^{4-}] + k_{HZ}[CuL^{2+}][HZ^{3-}]$ for macrocyclic and linear systems. Cyclization of L^3 significantly decelerates the exchange rates. Of the macrocyclic homologues, L^2 undergoes much slower displacement than L^1. The displacement of macrocyclic triamines is explained by a normal ligand-exchange reaction mechanism taking into account the "multiple juxtapositional fixedness" effect.

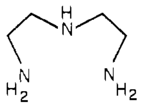
Kinetic behaviors of saturated macrocyclic polyamines at their metal complex formation and dissociation have drawn considerable attention recently in connection with their unusual thermodynamic stabilities.[2–6] The effects of cyclic structure, ring size, ring flexibility, and number of N donor atoms on the complex stability should be closely linked with magnitude and pH dependence of the formation and dissociation rate constants as well as with the reaction mechanisms. However, much of the investigation had been limited to the formation process, and few studies[2,3] have been made on the dissociation kinetics that are predicted to be more influential than the formation kinetics on the macrocyclic complex stability.[4–6] We now wish to report some kinetic behaviors of macrocyclic triamine ligands 9-membered 1,4,7-triazacyclononane (L^1) and 10-membered 1,4,7-triazacyclodecane (L^2) in reference to a linear counterpart dien (L^3) in their dissociation from copper(II) complexes.



L^1



L^2



L^3

Previous equilibrium studies[5,7–11] showed that both the linear and cyclic triamines form stable 1:1 Cu(II) complexes in aqueous solutions. The linear L^3 and macrocyclic L^1 complexes interestingly demonstrated similar stability constants.[5,7–9] The macrocyclic homologue L^2 forms a little less stable complex than L^1 or L^3.[11,12] We were thus interested to see how such results in the complexation equilibrium are manifested in dissociation kinetics. Should the "multiple juxtapositional fixedness effect" proposed for inertness of unsaturated macrocyclic triamines[13] be also operative in the saturated system, its quantitative estimation might be possible.

The present work measures the rates k_f of the ligand-exchange reaction (eq 1) of a copper(II) macrocyclic triamine (L) with ethylenediaminetetraacetate ion (EDTA) and *trans*-1,2-diaminocyclohexane-*N*,*N*,*N'*,*N'*-tetraacetate ion (CyDTA) (represented by the general term Z). Dissociation of CuL^{2+} macrocyclic complexes in aqueous solution (i.e. replacement of L by Z = H_2O) in general is extremely unfeasible and slow.[4] However, with use of Z = a multidentate ligand such as EDTA or CyDTA, the replacement of macrocyclic triamines becomes thermodynamically much more favorable and the rate becomes much faster, requiring stopped-flow techniques to study. For L = linear polyamine L^3, the reverse rates k_r of (1) have been already reported,[14] so that k_f values to be compared with are calculable by using the known stability constants. In our previous kinetic study[6] of L = macrocyclic tetra- and pentaamines in the exchange reaction (1) with Z = EDTA, the equilibrium is much favored to the reverse direction and we have measured the rates k_r. With all the relevant equilibrium constants known, the opposite rates k_f are calculated for comparison with the triamine macrocycle system. All the rate values are listed in Table II.

$$CuL^{2+} + Z \underset{k_r}{\overset{k_f}{\rightleftharpoons}} CuZ^{2-} + L \tag{1}$$

Experimental Section

The macrocyclic triamines L^1 and L^2 were prepared as described previously.[5,11] CyDTA and EDTA were purified by recrystallization as the free acid. Cu–L complex solutions were prepared by mixing a stock solution of copper(II) nitrate (standardized against EDTA) and L (~20% molar excess) in ammonia buffers ($9 < pH < 10.5$). Use of an excess L did not interfere with the exchange reaction rates. Typical concentrations were $[Cu^{2+}]_{ap} = 2 \times 10^{-3}–10^{-2}$ M, $[L]_F = 5 \times 10^{-4}–2 \times 10^{-3}$ M, $[Z]_F = 5 \times 10^{-3}–5 \times 10^{-2}$ M, and $[NH_3]_{total} = 6 \times 10^{-2}–3 \times 10^{-1}$ M. Constant ionic strength *I* was maintained at 0.2 M with $NaClO_4$. All the work was at 25.0 ± 0.1 °C. The data associated with protonation constants are based on pH readings. The equilibrium data used for the calculation are summarized in Table I.

Kinetic runs were followed spectrophotometrically by measuring the increase in absorbance due to the formation of CuZ species at the wavelength 750 nm for CyDTA and for EDTA on a Union Giken stopped-flow instrument. The reaction rates were determined by the second-order (unequal concentrations) plots except for L^2–CyDTA reaction which was treated by the initial slope method (for the first 30% of reaction).

Result and Calculation

Exchange Equilibria. The reaction (1) in ammonia buffers would involve mixed-ammonia complexes such as $Cu(NH_3)L^{2+}$ (as proved in the kinetic experiments, see the succeeding section) and $Cu(NH_3)Z$.[15] The multiple equilibria of (2) are

$$\begin{tikzcd}
CuL^{2+} + Z^{4-} \arrow[r, shift left, "K"] \arrow[d, shift right, "K^{NH_3}_L"'] & CuZ^{2-} + L \arrow[l, shift left] \arrow[d, shift right] \\
Cu(NH_3)L^{2+} \arrow[u, shift right] & Cu(NH_3)Z \arrow[u, shift right, "K^{NH_3}_Z"']
\end{tikzcd} \tag{2}$$

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Table I. Summary of Equilibrium Constants Used for the Present Study (All Data at $I = 0.2$ M and 25 °C)

	ligand					
	L^1 [a]	L^2 [b]	L^3 [c]	CyDTA[c]	EDTA[c]	NH_3[d]
protonation const						
$\log K_1$	10.59	10.85	9.93	11.43	9.80	9.26
$\log K_2$	6.88	6.76	9.05	5.93	6.12	
$\log K_3$	0.80	0.71	4.02	3.41	2.56	
$\log K_4$				2.39	1.96	
$\log K_{CuX}$	16.2	14.4	16.0	20.7	18.2	4.13 $\log \beta_2 = 7.61$ $\log \beta_3 = 10.48$ $\log \beta_4 = 12.59$
equilibrium const						
$\log K^{NH_3}{}_X$	1.19[e]	1.2[e]		1.55[f]	1.98[f]	

[a] Reference 5. [b] Reference 11. [c] References 14 and 16. The given values are corrected to $I = 0.2$ M. [d] A. Ringbom, "Complexation in Analytical Chemistry", Wiley, New York, 1963. [e] This work. [f] Reference 15.

expected to be occurring in the reaction mixture. The equilibrium constant K in (2) is immediately expressed as

$$K = \frac{K_{CuZ}(\alpha_H)_L(1 + K^{NH_3}{}_Z[NH_3])}{K_{CuL}(\alpha_H)_L(1 + K^{NH_3}{}_L[NH_3])} \quad (3)$$

where

$$(\alpha_H)_L = [L]_F/[L] = 1 + K_1[H^+] + K_1K_2[H^+]^2 + K_1K_2K_3[H^+]^3 \quad (4)$$

$$K^{NH_3}{}_L = [Cu(NH_3)L^{2+}]/[CuL^{2+}][NH_3] \quad (5)$$

and so forth. The replacement of L by Z in all the cases are thermodynamically very favorable and nearly complete under the reaction conditions employed. The logarithms of the conditional equilibrium constants K are calculated as 2.6 (L^1–EDTA), 3.7 (L^1–CyDTA), 3.8 (L^2–EDTA), and 4.9 (L^2–CyDTA) at pH 9 and $[NH_3] = 0.1$ M, and these values are even more at pH 10.5.

The fact that copper(II) initially is present exclusively in the form of CuL^{2+} and $CuL(NH_3)^{2+}$ (coordinated H_2O's are omitted) in ammonia buffer is ascertained by consideration of equilibrium 6. The conditional equilibrium constant K'

$$\Sigma_0^4Cu(NH_3)_i^{2+} + L \overset{K'}{\rightleftharpoons} CuL^{2+} + CuL(NH_3)^{2+} \quad (6)$$

is expressed as

$$K' = \frac{[CuL^{2+}] + [CuL(NH_3)^{2+}]}{[L]_F\{[Cu^{2+}] + [Cu(NH_3)^{2+}] + ... + [Cu(NH_3)_4{}^{2+}]\}} = \frac{K_{CuL}(1 + K^{NH_3}{}_L[NH_3])}{(\alpha_H)_L\beta_{NH_3}} \quad (7)$$

where

$$\beta_{NH_3} = 1 + \beta_1[NH_3] + ... + \beta_4[NH_3]^4 \quad (8)$$

In the case of L^2 solution at pH 9.3, $[NH_3]_{tot} = 0.1$ M, and $[L]_F = 10^{-3}$ M, $(\alpha_H)_L = 40$, $\beta_{NH_3} = 2.8 \times 10^7$, and $K^{NH_3}{}_L \cdot [NH_3] = 0.84$, so that the ratio $([CuL^{2+}] + [CuL(NH_3)^{2+}])/\Sigma_0^4[Cu(NH_3)_i^{2+}] = K'[L]_F$ is calculated as 4.1×10^2. Namely, copper complex of L^2 including a ternary complex with NH_3 is 410 times as much abundant as complexes of NH_3. With L^1, the K_{CuL} value is larger, and so the ratio of the macrocyclic complexes to the ammonia complexes is even larger.

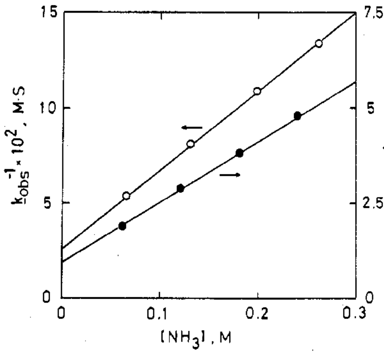
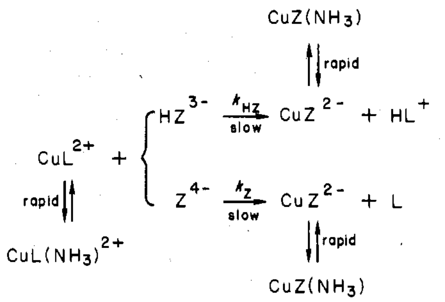


Figure 1. Determination of $K^{NH_3}{}_L$ by plots of eq 15: data for L^1 (○) at [CuL] = 4.0, $[L]_F = 0.5$, and [CyDTA] = 16.9 (all in 10^{-3} M) and pH 9.56; data for L^2 (●) at [CuL] = 4.0, $[L]_F = 0.5$, and [CyDTA] = 16.9 (all in 10^{-3} M) and pH 9.40.

Exchange Kinetics. The second-order kinetics (first order in $[Cu^{2+}]_{ap}$ and first order in $[Z]_F$) were observed in all the exchange cases. The observed second-order rate constants k_{obsd} for all the reactions are dependent on pH and $[NH_3]_{tot}$, which conforms to the reaction scheme



(9)

The exchange rate is expressed in the form of

$$k_{obsd}[Cu^{2+}]_{ap}[Z]_F = k_Z[CuL^{2+}][Z^{4-}] + k_{HZ}[CuL^{2+}][HZ^{3-}] \quad (10)$$

where

$$[CuL^{2+}] = [Cu^{2+}]_{ap}/(1 + K^{NH_3}{}_L[NH_3]) \quad (11)$$

$$[Cu^{2+}]_{ap} = [CuL^{2+}] + [CuL(NH_3)^{2+}] \quad (12)$$

$$[Z^{4-}] = [Z]_F/(\alpha_H)_Z \quad (13)$$

$$[HZ^{3-}] = [Z]_F[H^+]K_1/(\alpha_H)_Z \quad (14)$$

and $[Z]_F$ is total concentration of uncomplexed Z. Appropriate combination of (10)–(14) leads to

$$k_{obsd} = \frac{k_Z + k_{HZ}[H^+]K_1}{(\alpha_H)_Z(1 + K^{NH_3}{}_L[NH_3])} \quad (15)$$

Equation 15 predicts that at constant pH the reciprocal of k_{obsd} is proportional to $[NH_3]$. This was found to be the case with CyDTA-exchange rates, as shown in Figure 1. The gra-

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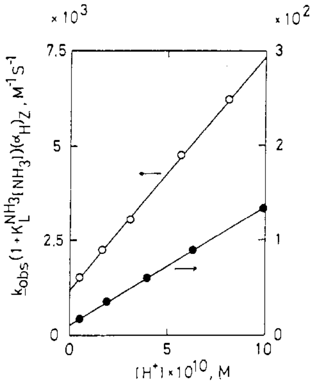

Figure 2. Determination of the rate constants k_Z and k_{HZ} by plots of eq 15 for L^1–CyDTA (○) at [CuL] = 4.0, $[L]_F$ = 0.5, [CyDTA] = 16.9, and $[NH_3]_{total}$ = 131 (all in 10^{-3} M) and for L^2–CyDTA (●) at [CuL] = 4.0, $[L]_F$ = 1.0, [CyDTA] = 16.9, and $[NH_3]_{total}$ = 240 (all in 10^{-3} M).

Table II. Summary of the Rate Constants (All in $M^{-1}\ s^{-1}$) at I = 0.2 M and 25 °C

	Z = EDTA		Z = CyDTA	
	k_{EDTA}	$k_{H(EDTA)}$	k_{CyDTA}	$k_{H(CyDTA)}$
L^1 [a]	2.2×10^4	7.3×10^4	1.0×10^3	2.0×10
L^2 [a]	2.5×10^2	2.9×10^2	1.1×10	4.6×10^{-1}
L^3 [b]			1.0×10^7	5.3×10^4
trien[b]	1.1×10^4	4.8×10^2	2.2×10^2	4.5×10^{-1}
1,4,7,10-tetraazacyclotridecane[c]	4.0×10^{-10}		4.3×10^{-9}	
1,4,8,12-tetraazacyclopentadecane[c]	1.6×10^{-4}		6.3×10^{-4}	
tetren[c,d]	2.2×10	9.7	7.9×10^{-1}	1.6×10^{-3}
1,4,7,10,13-pentaazacyclopentadecane[c]	3.2×10^{-8}	2.9×10^{-7}		

[a] This work. Average of at least three determinations. Error limits in k are ±10%. [b] Calculated by using the data in ref 14. trien = triethylenetetramine. [c] Reference 6. tetren = tetraethylenepentamine. [d] Reference 16.

dient/intercept of the linear relations gave $K^{NH_3}{}_L$; the value for L^1 is 1.55 × 10 and that for L^2 is 1.67 × 10. The $K^{NH_3}{}_L$ value for L^2 (=1.69 × 10) was checked by using the EDTA-exchange rates, which agrees very well with the value of 1.67 × 10 obtained at CyDTA exchange.

From pH dependence of k_{obsd} at given $[NH_3]_{tot}$, which are linear as shown in Figure 2, k_Z (=intercept) and k_{HZ} (=gradient/K_1) were determined. All the rate constants obtained this way are summarized in Table II in comparison with the relevant values for L^3.

Discussion

The resolved rate law for the macrocyclic L^1 and L^2 ligand-exchange reactions are the same as those established for the linear L^3 [14] and longer polyamines.[16] The second-order constants k_Z and k_{HZ} for the macrocyclic system likewise are significantly affected by the kind of leaving L and attacking Z. These overall kinetic pictures appear compatible with the mechanism (16) proposed for a linear system,[17] in which replacement reactions proceed via intermediates L′–M–Z′ comprising L and L on the metal ion (or some form of mixed-ligand complex) at the transition state.

$$ML^{2+} + Z \underset{}{\overset{\text{fast}}{\rightleftharpoons}} L'\text{–}M\text{–}Z' \xrightarrow{k_{rds}} MZ^{2-} + L \qquad (16)$$

As suggested for Ni^{2+}–polyamine reactions with EDTA,[18] the reaction intermediates L′–M–Z′ would be coordinated with three nitrogens of L^1–L^3 (facially with L^1 and L^2 and meridionally with L^3).[6–9] Faster exchange reactions of macrocyclic triamine L^1 than of tetraamines (linear trien or macrocycles) imply that the lack of the fourth N coordination is very important for the transition states, which is compatible with the observation that $CuL(NH_3)^{2+}$ (H_2O's to fill the coordination sites are neglected for simplicity in this paper) is not a reactive species. Interaction of Z with the remaining equatorial positions would be sterically unfavorable. On the other hand, CuL^{2+} has two equatorial vacancies which would allow strong association of Z, including possible Cu–N bonding.

Comparison of the rate constants for CyDTA replacement reactions in Table II clearly demonstrates kinetic effects of the ligand cyclization found in the substitution reactions. The inertness toward substitution is thus measured quantitatively, which may be rationalized by the MJF effect.[13] For release of the linear ligands L from the intermediates L′–M–Z′, dissociation of N donor atoms on L′ and replacement by donor atoms on Z would proceed in stepwise fashions, whereby the slowest step for L^3 most likely involves the dissociation of the first Cu–N bond, which determines the overall exchange rates. The stepwise mechanism as such would be unlikely with the macrocycles due to their rigid placement onto Cu (although containing a weak Cu–N (axial) bond). Instead, multiple dissociation of Cu–N bonds should proceed to Z chelation, during which new bond formation including supplementary aquation would be difficult to occur (due to steric effects etc.) to offset the loss of the stability of the intermediates, as in the case of the linear system. Thus, higher activation energy would be required, resulting in the slower macrocycle displacement reactions.

It is of interest that the substitution rates for L^1 and L^2 (compare, for example, k_{CyDTA} values in Table II) are not relevant to the thermodynamic stability constants of the starting CuL^{2+} complexes (see Table I). This may be interpreted as follows:

The experimental rate constants k_{exptl} for the reaction mechanism (16) are expressed as

$$k_{exptl} = k_{rds}K_{ML'}K_{MZ'}/K_{ML} \qquad (17)$$

where ML′ and MZ′ represent coordinated L and Z segments, respectively, in the intermediates L′–M–Z′. Between the homologous L^1 and L^2, the magnitude of $K_{MZ'}$ would be similar. The irrelevance of k_{exptl} values with K_{ML} may be accounted for by the rate-determining step occurring at an early stage of L unwrapping, i.e., $K_{ML'} = K_{ML}$ in eq 17. The faster displacement of L^1 relative to L^2, i.e. k_{rds} for L^1 > k_{rds} for L^2, may reflect greater steric constraint of the L^1 intermediate, which may be supported by the fact that Cu–L^1 complex formation is enthalpically less favorable than Cu–L^2 formation due to weaker coordinate bond strength.[11]

Registry No. CyDTA, 13291-61-7; EDTA, 60-00-4; $Cu(L^1)^{2+}$, 64560-64-1; $Cu(L^2)^{2+}$, 67163-01-3.

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