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Kinetic Study of Replacement Reactions of Cyclic Polyethers by a Cyclic Tetraamine in Lead(II) Complexes in Acetate Buffers

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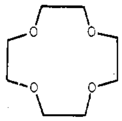
The kinetics of ligand–ligand replacement have been studied polarographically for the reaction of a 12-membered macrocyclic tetraamine (L) with Pb^{2+} complexes of polyethers (Y) including a linear pentaether (V) and macrocyclic 12-membered tetra- (I), 15-membered penta- (II), 18-membered hexa- (III), and 24-membered octaethers (IV) in acetate buffers at $I = 0.1$ M and 25 °C. The formation of PbL^{2+} is first order in [L] and first order in $[Pb(OAc)^+]$ and simultaneously in $[PbY^{2+}]$. The rates are resolved into those with mono- (HL^+) and diprotonated tetraamine species (H_2L^{2+}). The relative rates of the replacement of Y by L are approximately inversely proportional to the relative stabilities of the PbY^{2+} complexes, with III being replaced most slowly. Mixed complexes are proposed as the reaction intermediates prior to the rate-determining step. The observations are linked to the dependence of the complex stability constants upon the size of the cyclic ring, i.e., the cation selectivity of the cyclic polyethers.

The selectivity shown by certain cyclic polyethers toward cations is well documented. The demonstration of cation selectivity by these compounds has resulted in much interest in them for possible use in many areas where this property is important. While much equilibrium work has already been done,[2] kinetic data[3] are still deficient despite their fundamental importance for understanding and applications of the cation selectivity.

In this paper, we report results of a kinetic study of ligand replacement of cyclic polyethers I–IV and a linear pentaether V by a cyclic tetraamine L in lead(II) complexes according to eq 1(where Y denotes a polyether and the degree of protonation to L is not indicated).

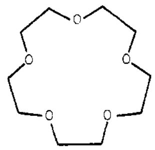
$$PbY^{2+} + L \xrightarrow{k} PbL^{2+} + Y \qquad (1)$$

The use of a series of structurally related polyether ligands might provide some pictures about the nature of the rate-determining step of the ligand-exchange reactions involving dissociation of the polyethers. That might help elucidate the mechanism by which the selective binding of the cyclic polyethers to cations occurs.



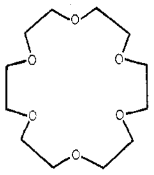
I

12-crown-4



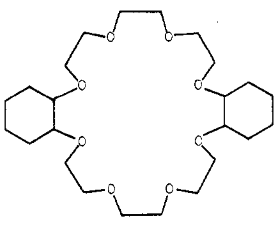
II

15-crown-5



III

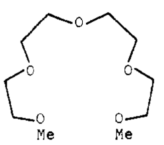
18-crown-6



IV

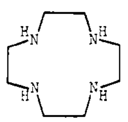
dicyclohexyl-

24-crown-8



V

tetraglyme



L

cyclen

The reactions (1) were conducted in acetate buffers, where (i) the conditional stability constant of the product PbL^{2+} is much larger than those of the reactant PbY^{2+},[4,5] (ii) the disappearing PbY^{2+} (in equilibrium with aqua and acetate complex species) and the appearing PbL^{2+} in the course of the reaction are easily discerned on polarograms, and (iii) the rates of the ligand–ligand exchanges are moderate. Hence, we have employed a polarographic method to pursue the kinetics, as so done on PbL^{2+} complexation from a $Pb(OAc)^+$ reactant.[4] Before running the kinetics, we determined the formation constants for Pb^{2+}–I, –II, and –IV polarographically.

Experimental Section

The cyclic polyethers I (Borregaard A.S, Norway), IV (Nisso, Japan), and the linear ether V (Tokyo Kasei, Japan) were used without further purification. II (Nisso, Japan) and III (Aldrich, U.S.A.) were purified by the methods described in literatures.[2a,3g] The cyclic tetraamine L was synthesized using the method of Richman and Atkins.[6] The protonation constants of L determined previously (at $I = 0.2$ M)[4,7] were corrected to $I = 0.1$ M: $\log K_1 = 10.72$ and $\log K_2 = 9.77$. A standard Pb^{2+} solution was prepared by dissolving $Pb[NO_3]_2$ (analytical grade) in redistilled water. Tetraethylammonium perchlorate (TEAP) was prepared by the method of Fujinaga et al.[8] Acetate buffer was prepared from acetic acid and tetraethylammonium hydroxide (analytical grade). The total ionic strength (I) of 0.1 M was made up with TEAP.

The equilibrium[5] and kinetic experiments[4] were performed in a polarographic apparatus using the general approach outlined in previous papers. A decrease in reduction wave height of PbY^{2+} in acetate buffers was observed as the PbL^{2+} complex formed. The observed second-order rate constants were determined by the initial-gradient method. Under the experimental conditions (see Table II), the 50% substitution required ca. 120, 150, 1200, 70, and 120 s for I, II, III, IV, and V, respectively.

Results and Discussion

Formation Constants of PbY^{2+}. Data for Y = III and V have been previously given.[5] In the present experiments the data for I, II, and IV were obtained.

Pb^{2+} ions (ca. 2×10^{-4} M) in the solutions containing I or II (ca. 10^{-2}–10^{-1} M) at pH 2.0 (adjusted with $HClO_4$) and 25 °C gave reversible polarographic waves at the dropping mercury electrode. Complexation of PbY^{2+} was demonstrated by the negative shift of $E_{1/2}$, $\Delta E_{1/2}$, upon increasing the concentration of Y. A linear relation between antilog $[\Delta E_{1/2}/0.0296 + \log (k_{Pb}/k_{PbY})]$ and [Y] for both I and II (Figure 1) indicates formation of only the 1:1 complexes, where the log of the diffusion current constant ratio, k_{Pb}/k_{PbY}, was 0.10. The stability constants, K_{PbY}, were estimated from the gradients. An identical treatment was applied to Y = III previously.[5]

For determination of K_{PbY} for Y = IV, we used the method of Kacěna and Matoušek,[9] since the solutions containing IV exhibited irreversible reduction waves. The mean diffusion constant $\bar{D}$ of the simultaneously diffusing free and complexed

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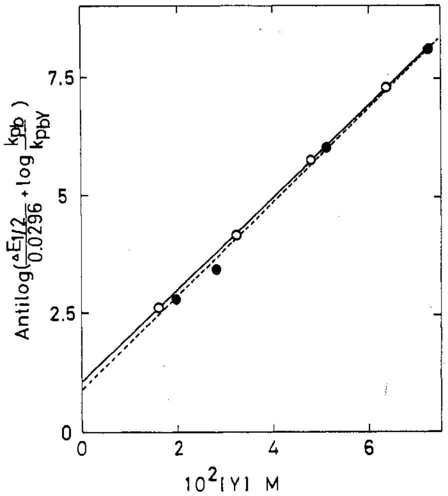


Figure 1. Determination of K_{PbY} for Y = I (○) and Y = II (●) by plots of antilog ($\Delta E_{1/2}$/0.0296 + log (k_{Pb}/k_{PbY})) against 10^2[Y]. Data at $[Pb^{2+}] = 2 \times 10^{-4}$ M, pH 2.00, I = 0.1 M, and 25 °C.

Table I. Stability Constants of Lead(II)–Polyether Complexes. log K_{PbY} and Resolved Rate Constants k_H' and k_{2H}' (M^{-1} s^{-1}) for PbL^{2+} Complex Formation from PbY^{2+} and L at I = 0.1 M and 25 °C

Y	log K_{PbY}[b]	k_H'[c]	k_{2H}'[c]
I	2.00	2.1×10^5	1.5×10
II	2.05	1.8×10^5	2.1
III	4.4[a]	7.7×10^2	3.5×10^{-2}
IV	2.54	9.1×10^4	3.7
V	0.5[a]	6.3×10^5	2.0×10

[a] From ref 5. [b] ±0.05. [c] ±0.5.

Pb^{2+} is expressed in terms of diffusion constants of free (D_{Pb}) and complexed Pb^{2+} (D_{PbY}) and K_{Pby} by

$$\bar{D} = \frac{D_{Pb} + D_{PbY}K_{PbY}[Y]}{1 + K_{PbY}[Y]} \qquad (2)$$

This is transformed into (3) by application of the Ilkovic

$$K_{PbY}[Y] = \frac{D_{Pb} - \bar{D}}{\bar{D} - D_{PbY}} = \frac{(i_d)_{Pb}{}^2 - i_d{}^2}{i_d{}^2 - (i_d)_{PbY}{}^2} \qquad (3)$$

equation at constant concentration of the metal ion. Here, $(i_d)_{Pb}$ and $(i_d)_{PbY}$ are diffusion currents of free and complexed metal ions, respectively. The $(i_d)_{PbY}$ value was estimated by extrapolating the observed diffusion current (i_d) at Y = ∞. The K_{PbY} was determined from the slope of the linear relation in Figure 2.[10] All the results are summarized in Table I.

To our knowledge, the K_{PbY} values for Y = I and IV have not been reported. For Y = II, the log K_{PbY} value of 1.85 (at I 0.1 M and 25 °C) had previously been determined calorimetrically by Izatt et al.,[2b] which agrees fairly well with our value of 2.05 (at I 0.1 M and 25 °C). We used our value for the following kinetic study.

It is of interest that relatively big Pb^{2+} forms a complex with the 12-membered tetraether I as stable as that with the 15-membered pentaether II, although less favorable complexation might be anticipated based on the cavity–cation size consideration. Temperature dependence of K_{PbI} gave $\Delta H = -1.8$ kcal mol^{-1} and $\Delta S = 3$ cal K^{-1} mol^{-1} (because of a very small gradient, the accuracy is limited), as compared with $\Delta H = -3.6$ kcal mol^{-1} and $\Delta S = -2.5$ cal K^{-1} mol^{-1} for Pb–II,[2b] indicating a significant contribution of favorable entropy change to the stability of the Pb–I complex. The less favorable complexation of 24-membered IV with respect to 18-membered III may arise from the need for large conformational changes to accommodate the relatively small Pb^{2+}. Similar trends were already reported for alkali metal ion complexes.[2c]

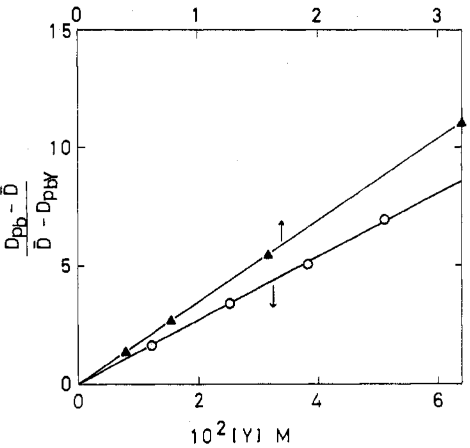
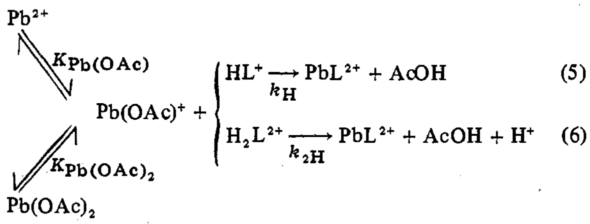


Figure 2. Determination of K_{PbY} for Y = I (○) and Y = IV (▲) by plots according to eq 3. Data at $[Pb^{2+}] = 2 \times 10^{-4}$ M, pH 2.00, I = 0.1 M, and 25 °C.

Ligand Replacement Kinetics. Earlier,[4] we measured the rate of complexation of Pb^{2+} with L in acetate buffers. The observed second-order rate constants k (first order in $[Pb^{2+}]_i$ and first order in $[L]_i$) were resolved into k_H and k_{2H} (due to the reaction of $Pb(OAc)^+$ with HL^+ and H_2L^{2+}, respectively) from their dependence on pH and [AcO^-] according to expression (4), and the results were interpreted in the reaction scheme (5) and (6). Here $(\alpha_H)_L = [L]_f/[L]$, $[L]_f = [L] + [HL^+] + [H_2L^{2+}]$ etc., $\beta_{AcO} = [Pb^{2+}]_f/[Pb^{2+}(aq)] = 1 + K_{Pb(OAc)}[AcO^-] + K_{Pb(OAc)}K_{Pb(OAc)_2}[AcO^-]^2$, $[Pb^{2+}]_f = [Pb^{2+}(aq)] + [Pb(OAc)^+] + [Pb(OAc)_2]$, and K_i is the ith protonation constant (note: in ref 7, K_i stood for the ith ionization constant).

$$k = \frac{K_{Pb(OAc)}[AcO^-]}{(\alpha_H)_L\beta_{AcO}}(k_HK_1[H^+] + k_{2H}K_1K_2[H^+]^2) \qquad (4)$$

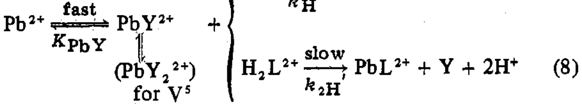


$$Pb^{2+} \underset{}{\overset{K_{Pb(OAc)}}{\rightleftharpoons}} Pb(OAc)^+ \underset{}{\overset{K_{Pb(OAc)_2}}{\rightleftharpoons}} Pb(OAc)_2$$

$$Pb(OAc)^+ + \begin{cases} HL^+ \xrightarrow[k_H]{} PbL^{2+} + AcOH & (5) \\ H_2L^{2+} \xrightarrow[k_{2H}]{} PbL^{2+} + AcOH + H^+ & (6) \end{cases}$$

In the present reactions of Pb^{2+} with L in acetate buffers containing a cyclic or a linear polyether Y, the observed rate constants k' are first order in $[Pb^{2+}]_i$ and first order in $[L]_i$ (experimented with $[Pb^{2+}]_i$ and $[L]_i$ over a three- to fivefold range). The k' values are dependent on pH, [AcO^-], and [Y] (Table II), and, moreover, $k'(\alpha_H)_L(\beta_{AcO} + K_{PbY}[Y]_f)K_1^{-1}\cdot[H^+]^{-1}$ (this term is called A) is always larger than $K_{Pb(OAc)}[AcO^-](k_H + k_{2H}K_2[H^+])$ (term B). These facts suggest that the complexation of L occurs simultaneously through Pb–OAc and Pb–Y species. It was further found that plots of ($A - B$) against [H^+] give straight lines with intercepts of finite values for I–V (Figure 3).

We propose complexation pathways (7) and (8) along with (5) and (6).[11] Rate equation 9 is then derived in terms of A and B (note that the rate expression (4) is written as $A = B$ where [Y] = 0). The individual rate constants k_H' and k_{2H}'



$$Pb^{2+} \underset{K_{PbY}}{\overset{fast}{\rightleftharpoons}} PbY^{2+} \; (\rightleftharpoons (PbY_2{}^{2+}) \text{ for } V^5) + \begin{cases} HL^+ \xrightarrow[k_H']{slow} PbL^{2+} + Y + H^+ & (7) \\ H_2L^{2+} \xrightarrow[k_{2H}']{slow} PbL^{2+} + Y + 2H^+ & (8) \end{cases}$$

$$A = B + K_{PbY}[Y]_f(k_H' + k_{2H}'K_2[H^+]) \qquad (9)$$

Table II. Dependence of Initial Rates on Concentrations of Acetate and Polyethers for Complex Formation of PbL^{2+} at I = 0.1 M and 25 °C

Y	$10^3[Pb^{2+}]_i$, M	$10^3[L]_i$, M	pH	$10^3[AcO^-]$, M	$10^3[Y]$, M	k'(obsd), $M^{-1} s^{-1}$	k'(calcd), $M^{-1} s^{-1}$
I	0.19_2	0.41_8	4.92	48.1	70.4	$14._4$	14.4
				48.1	35.2	$13._1$	13.4
				96.2	70.4	$13._7$	13.5
II	0.19_2	0.38_5	4.91	38.5	44.4	8.5_8	9.0
				38.5	88.8	6.8_6	7.7
				76.9	44.4	$10._4$	10.5
III	0.19_2	0.41_8	5.17	35.0	15.0	0.36	0.37
				35.0	30.0	0.22	0.21
				70.0	15.0	0.65	0.67
IV	0.19_2	0.41_8	4.99	48.1	10.0	$11._0$	11.1
				48.1	30.0	8.8	9.0
				96.2	10.0	$11._8$	11.7
V	0.19_2	0.38_5	4.88	38.5	300	7.2_4	7.24
				57.7	300	7.9_7	8.04
				96.2	300	8.6_9	8.54
				96.2	1000	3.6_2	3.49

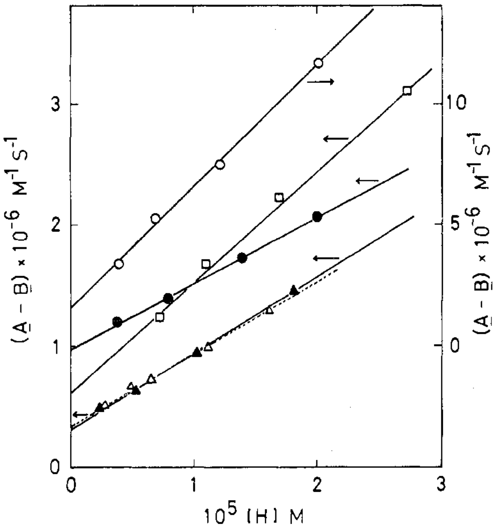


Figure 3. Determination of k_H' and k_{2H}' by plots according to eq 9 at I = 0.1 M and 25 °C: Y = I (○) at $[Pb^{2+}] = 0.19_2$, [Y] = 70.4, $[AcO^-]$ = 48.1, and $[L] = 0.38_5$ mM; Y = II (●) at $[Pb^{2+}] = 0.19_2$, [Y] = 48.1, $[AcO^-]$ = 38.5, and $[L] = 0.38_5$ mM; Y = III (△) at $[Pb^{2+}] = 0.19_2$, [Y] = 15.0, $[AcO^-]$ = 35.0, and $[L] = 0.41_8$ mM; Y = IV (▲) at $[Pb^{2+}] = 0.19_2$, [Y] = 10.0, $[AcO^-]$ = 48.1, and [L] $= 0.38_5$ mM; and Y = V (□) at $[Pb^{2+}] = 0.19_2$, [Y] = 300, $[AcO^-]$ = 19.2, and $[L] = 0.38_5$ mM.

for the reactions of PbY^{2+} with HL^+ and H_2L^{2+}, respectively, are determined from the intercepts and gradients of the linear plots (at given values of $[AcO^-]$ and [Y]) in Figure 3. The k_H and k_{2H} value used for the calculation are, respectively, 8.3×10^5 and 1.4 $M^{-1} s^{-1}$.[4] The $K_{Pb(OAc)}$ value is $10^{2.11}$.[12] The results are summarized in Table I. The rate constants k' were calculated using the resolved k_H' and k_{2H}' at different concentrations of acetate and of Y. The calculated values k'(calcd) are in good agreement with the observed values k'(obsd) as shown in Table II.

The rate law for the reactions involving the polyether–L exchanges implies that the lead ions exist as mixed complexes containing Pb–O and Pb–N bonds in the activated complexes. A comparison of the individual rate constants k_H' or k_{2H}' for the cyclic and linear polyethers investigated shows that the 18-membered macrocycle III is displaced most slowly. Furthermore, the relative rates of the replacement by L are approximately in inverse proportion to the relative stabilities of the PbY^{2+} complexes. This observation is interpreted in that the major segments of Y are decomplexed in the intermediate complexes. The subsequent rearrangement of the coordination shell with the total loss of Y to be occupied by L must take place during the rate-determining step.[13] In this parallel mechanism throughout for I–V, the identity of the attacking ligand would have only a small effect on the relative exchange rates. In the large ring system IV or linear system V, the flexible configurations would invite facile partial displacement to form the stable intermediates, while in the small ring system I or II, their ether oxygens are arranged at one side of the cation leaving the other side open for the ready attack of L. Intermediate III is less likely to form a stable mixed–complex species, since the III having the right size for the metal ion might rigidly surround it in a plane and allow limited space for the entry of the bulky L and also have little of the configurational flexibility needed for the decomplexation. If the present observation is extrapolated to the now accepted notion[3b,f,g] that the relative stabilities of macrocyclic complexes are predominantly determined by the rates of decomplexation, one can conclude that it is the initial stage of the decomplexation mainly associated with conformational changes that is critical for the cation selectivity. This conclusion is in accord with the one derived from the kinetic study of macrocyclic polythioethers by Rorabacher et al.[14]

The magnitudes of the resolved rate constants k_H' and k_{2H}' for polyether (free from the cyclization effect, such as V) displacement are not essentially different from those of k_H and k_{2H} for acetate displacement. A similar mechanism of complexation of L would be prevalent, which was previously discussed.[4]

Registry No. PbY^{2+} (Y = I), 67011-19-2; PbY^{2+} (Y = II), 61059-93-6; PbY^{2+} (Y = III), 61060-01-3; PbY^{2+} (Y = IV), 66966-30-1; PbY^{2+} (Y = V), 66966-31-2; L, 294-90-6.

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(10) log K_{PbY} of 2.14 for Y = I was obtained by this method, which agrees with the value of 2.00 obtained above.
(11) We ignored participation of $Pb(OH)^+$ species as another Pb^{2+} reactant, in view of the acid ionization constant, pK_a, of 6.9 (L. G. Sillen and A. E. Martell, "Stability Constants of Metal Ion Complexes", 2nd ed, The Chemical Society, London, 1964) for the aqua lead ion and the experimental conditions of pH ca. 5. Assuming the same rate constants to be applied as found for $Pb(OAc)^+$ (both species having the same charge), the contribution of this pathway is negligible (less than 1%) to the net rate.
(12) N. Tanaka and K. Kato, *Bull. Chem. Soc. Jpn.*, **33**, 417, 1412 (1960).
(13) It is of interest to note that various aminocarboxylate ligands in Cu^{2+} complexes are replaced by a 13-membered cyclic tetraamine analogue, whose relative rate constants are also inversely proportional to the stabilities of the aminocarboxylate complexes. Mixed complexes were similarly proposed as the intermediates prior to the rate-determining step (M. Kodama and E. Kimura, *J. Chem. Soc., Dalton Trans.*, 247 (1978). It is also interesting that the aminocarboxylate ligands on Pb^{2+} ions are replaced with other aminocarboxylates in a similar reaction mechanism (J. D. Carr, K. Torrance, C. J. Cruz, and C. N. Reilley, *Anal. Chem.*, **39**, 1358 (1967); J. D. Carr and D. R. Baker, *Inorg. Chem.*, **10**, 2249 (1971)).
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Nucleophilic Displacement Reactions of Bis(triglycinato)cuprate(II) and Bis(glycinamide)copper(II)

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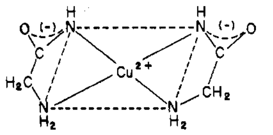
Bis(glycinamide)copper(II), $Cu(H_{-1}Ga)_2$, undergoes direct nucleophilic attack by triethylenetetramine (trien) with a rate constant of 1.4×10^4 M^{-1} s^{-1} at 25.0 °C. The trien reactivity with mono(triglycinato)cuprate(II), $Cu(H_{-2}G_3)^-$, is 3 orders of magnitude greater, but it is at least 2 orders of magnitude less with bis(triglycinato)cuprate(II), $Cu(H_{-1}G_3)_2^{2-}$, than with $Cu(H_{-1}Ga)_2$. Axial coordination of the carboxylate groups in $Cu(H_{-1}G_3)_2^{2-}$ is proposed. The reaction of *trans*-cyclohexanediaminetetraacetate, CyDTA, with $Cu(H_{-1}G_3)_2^{2-}$ proceeds by prior protonation of one peptide group to give $Cu(H_{-1}G_3)(G_3)^-$ followed by the formation of a ternary complex, $Cu(H_{-1}G_3)$CyDTA, with the displacement of one G_3^-. A similar path occurs with EDTA, but due to increased steric contraints CyDTA is 6×10^3 less effective as a nucleophile. The formation of $Cu(H_{-1}G_3)$CyDTA and the displacement of the second G_3^- to form $CuCyDTA^{2-}$ both contribute to the rate-limiting steps.

Introduction

The rates of ligand-exchange reactions of the doubly deprotonated tripeptide complexes of copper(II), $Cu(H_{-2}$tripeptide$)^-$, are very sensitive to steric factors in both the attacking nucleophile[1-3a] and the tripeptide.[3b] The planarity of the coordinated deprotonated-peptide groups causes substantial hindrance to the equatorial coordination of incoming ligands. As a result nucleophiles such as EDTA which contain tertiary amine groups are not very reactive. On the other hand, triglycine (G_3^-) catalyzes[3] the exchange reaction between $Cu(H_{-2}G_3)^-$ and EDTA by forming bis(triglycinato)cuprate(II), $Cu(H_{-1}G_3)_2^{2-}$. While EDTA appears to react more rapidly with $Cu(H_{-1}G_3)_2^{2-}$ than it does with $Cu(H_{-2}G_3)^-$, just the reverse is true for trien, a nucleophile with primary amine groups.

In the present work the kinetics and mechanism of the reaction of CyDTA (*trans*-1,2-diaminocyclohexanetetraacetate) with $Cu(H_{-1}G_3)_2^{2-}$ and of trien with bis(glycinamide)copper(II), $Cu(H_{-1}Ga)_2$, are reported. The CyDTA study helps to confirm the mechanism proposed for the EDTA reaction,[3] in which $[Cu(H_{-1}G_3)G_3]^-$ is the reactive species. Greater steric hindrance for CyDTA compared to EDTA greatly decreases its rate of attack on $[Cu(H_{-1}G_3)G_3]^-$ and hence shifts the rate-determining steps to later stages in the mechanism than is the case for EDTA. The $Cu(H_{-1}G_3)_2^{2-}$ complex itself is not very reactive toward any nucleophiles. By contrast trien reacts quite rapidly with $Cu(H_{-1}Ga)_2$. The bis(glycinamide) complex of copper(II) is known to be doubly deprotonated[4-6] and has the spectral characteristics of square-planar copper complexes.[6] Raman data suggest the cis geometry shown in structure I.[2] The bis(triglycine) complex also appears to prefer a cis configuration and a coordination geometry similar to that in structure I was proposed earlier.[2] However, the large difference in the trien reactivity with $Cu(H_{-1}Ga)_2$ and with $Cu(H_{-1}G_3)_2^{2-}$ leads to the proposal that the carboxylate groups in the bis(triglycine) complex are axially coordinated as shown in structure II. Other physical properties provide some supporting evidence for the proposed axial coordination.



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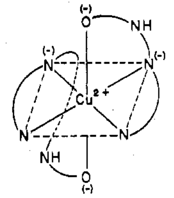

II

Experimental Section

Chromatographically homogeneous triglycine and glycinamide hydrochloride (Ga·HCl) were used without further purification. *trans*-1,2-Diaminocyclohexanetetraacetic acid was recrystallized as the monosodium salt and triethylenetetramine disulfate was twice recrystallized from ethanol–water. A stock 0.101 M $Cu(ClO_4)_2$ solution was prepared from the twice recrystallized salt and standardized with EDTA (murexide indicator).[7] The CyDTA and trien solutions were standardized by the mole ratio method against the Cu(II) solution and the copper(II)–triglycine and glycinamide solutions were freshly prepared prior to each day's experiments. The ionic strength was maintained at 0.20 M with $NaClO_4$. Hydrogen ion concentrations were calculated from the measured pH using the relationship $-\log [H^+] = pH - 0.14$.[8]

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