experiments. It should further be noted that, from the standpoint of the charge of the proposed SN1CB intermediate, the competition of NO_2^- with water might be expected to be less favorable for $Co(D_2H)(NO_2)^-$ than for $Co(NH_3)_4(NH_2)^{2+}$. In any case, the mechanistic ambiguity relating to possible contributions from SN2, SN2CB, and SN1CB paths to the base hydrolysis of $Co(DH)_2(NO_2)Br^-$ remains to be resolved.

Mechanism for the Proton-Transfer Reactions of a Peptide Hydrogen in Copper(II) Triglycine

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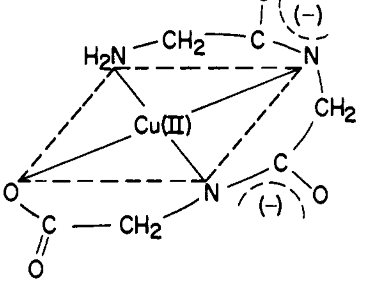
Abstract: The rate of interconversion of $CuH_{-2}L^-$ and $CuH_{-1}L$ (where L is triglycine and the protons are ionized from the peptide linkages) is much slower than normal acid–base reactions. The rate constant for the reaction of H_3O^+ with $CuH_{-2}L^-$ is 4.9×10^6 M^{-1} sec^{-1}, and the value for the reaction of OH^- with $CuH_{-1}L$ is 2.5×10^4 M^{-1} sec^{-1}. The reason proposed for the slower rates is the necessity to break and rearrange coordinate bonds to copper. The proton addition is general acid catalyzed and proton removal is subject to base catalysis. Two reaction paths are proposed. The copper–imide bond in $CuH_{-2}L^-$ is not easily broken and tends to dissociate after the addition of a proton to the peptide nitrogen.

Copper(II) complexes of short-chain polypeptides promote the ionization of the peptide hydrogens.[3-9] In the present work the speed and mechanism of this type of proton-transfer reaction is examined for copper(II) triglycine which forms $CuH_{-1}L$ (or CuA) and $CuH_{-2}L^-$ (or CuB^-) with the loss of one and two protons, respectively, from triglycine (L^-). The pK_a values for these ionizations are 5.4 and 6.6, and from infrared studies in D_2O it was concluded that the structure of $CuH_{-2}L^-$ can be represented by I.[9] The crystal structures of disodium tetraglycinocuprate(II) and of sodium triglycinocuprate(II) ($NaCuH_{-2}L \cdot H_2O$) have the peptide nitrogens coordinated to copper.[5,6,10] When copper triglycine is crystallized from acid solutions to give $CuLCl \cdot 1.5H_2O$, the peptide chain is attached to two copper atoms and each copper atom is bonded to two different peptide molecules. The copper is coordinated to the carbonyl oxygen of the peptide link.[5] Structures have been suggested for CuL^+ and for $CuH_{-1}L$ in solution where the -NH- group of the peptide link is coordinated.[9] Our kinetic evidence suggests that the proton-transfer reactions between $CuH_{-2}L^-$ and $CuH_{-1}L$ involve copper–nitrogen dissociation and that $CuH_{-1}L$ has carbonyl oxygen coordination.



I ($CuH_{-2}L^-$)

The reaction of H_3O^+ with $CuH_{-2}L^-$ to form $CuH_{-1}L$ is much less than the diffusion-controlled rate.[11] This proton-transfer reaction is general acid catalyzed and can be studied in the presence of ethylenediaminetetraacetate ion (EDTA) which does not react as a nucleophile with $CuH_{-2}L^-$ but does react with $CuH_{-1}L$. The reactions of $CuH_{-1}L$ with bases were studied directly using a pH-jump method.

Experimental Section

Kinetic runs were followed using stopped-flow spectrophotometers. One instrument was described earlier[12] and the other was a Durrum-Gibson stopped-flow, Durrum Instrument Corp., Palo Alto, Calif. Both instruments were thermostated at 25.0 ± 0.1°.

The reaction between copper triglycine and EDTA was followed by the disappearance of $CuH_{-2}L^-$ which has a much higher molar absorptivity than $CuH_{-1}L$ or $CuEDTA^{2-}$ at 555 mμ. This wavelength was used for reactions at pH 6.0–7.5 where a significant percentage of the copper triglycine is present as $CuH_{-1}L$. Above pH 7.5 the reactions were followed at 235 mμ.

Triglycine was obtained (chromatographically homogeneous) from Mann Research Laboratories (New York, N. Y.) and was used without further purification. A 9.85×10^{-2} M stock solution of $Cu(ClO_4)_2$ was prepared from the twice-recrystallized salt and standardized against EDTA. The copper(II)–triglycine complex was prepared for each series of reactions by mixing copper(II) and triglycine using a 2% molar excess of triglycine. The concentration of copper(II) triglycine used for a kinetic run ranged from 2 ×

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[1] Abstracted from the Ph.D. Thesis of G. K. P., Purdue University, June 1968.

[2] Address correspondence to this author.

[3] H. Dobbie and W. D. Kermack, *Biochem. J.*, **59**, 246, 257 (1955).

[4] A. R. Manyak, C. B. Murphy, and A. E. Martell, *Arch. Biochem. Biophys.*, **59**, 373 (1955).

[5] T. Cooper, H. C. Freeman, G. Robinson, and J. Schoone, *Nature*, **194**, 1237 (1962).

[6] H. C. Freeman and M. R. Taylor, *Proc. Chem. Soc.*, 88 (1964).

[7] W. L. Koltun, R. H. Roth, and F. R. N. Gurd, *J. Biol. Chem.*, **238**, 124 (1963).

[8] M. K. Kim and A. E. Martell, *Biochemistry*, **3**, 1169 (1964).

[9] M. K. Kim and A. E. Martell, *J. Am. Chem. Soc.*, **88**, 914 (1966).

[10] H. C. Freeman, J. C. Schoone, and J. G. Sime, *Acta Cryst.*, **18**, 381 (1965).

[11] G. K. Pagenkopf and D. W. Margerum, *J. Am. Chem. Soc.*, **90**, 501 (1968).

[12] D. W. Margerum and J. D. Carr, *ibid.*, **88**, 1639 (1966).

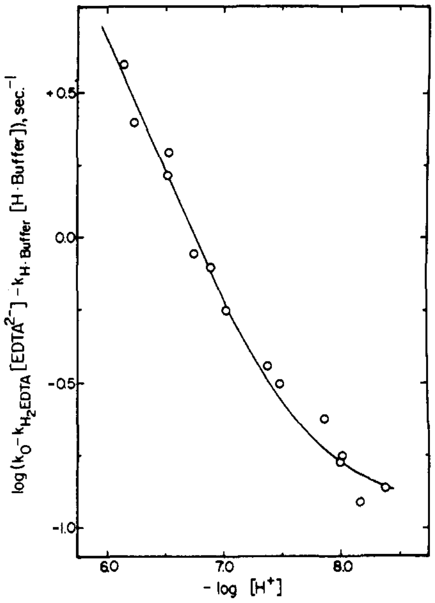

Figure 1. The effect of acidity on the rate of protonation of $CuH_{-2}L^-$. The observed first-order rate constant is corrected for the general acid catalysis of EDTA and buffer. The solid line is calculated from $k_H = 4.9 \times 10^6\ M^{-1}\ sec^{-1}$ and $k_d = 0.12\ sec^{-1}$ (see eq 5): 25.0°, $\mu = 0.10$.

10^{-5} to $2 \times 10^{-3}\ M$ depending on the wavelength and the cell path of the stopped-flow device (2 or 20 mm).

Ionic strength was maintained at 0.10 M with $NaClO_4$, and the hydrogen ion concentrations were calculated from pH measurements using $-\log [H^+] = pH - 0.11$,[13] and hydroxide ion concentrations were calculated from $pK_w = 13.78$.

Buffers were prepared from boric acid, 2,6-lutidine, and tris(hydroxymethyl)aminomethane (Tris). The buffer concentrations ranged from 4.0×10^{-3} to $1.25 \times 10^{-2}\ M$.

The acid species of EDTA and of the buffers contribute to the EDTA reaction with $CuH_{-2}L^-$. The rate constants for each species were determined by observing the rate as a function of the concentration of one acid while the concentrations of the other acids remained constant. The observed rates required stopped-flow techniques but were sufficiently slow to permit an excess of the acid species. The rate expression is

$$\frac{-d[CuH_{-2}L^-]}{dt} = k_0[CuH_{-2}L^-] \qquad (1)$$

where k_0 is a function of the general acid concentrations. For each acid several pH values were used to ensure the correct species assignment.

For the reactions of $CuH_{-1}L$ with bases the pH of the copper(II) triglycine solution was adjusted to about 6.8. At this pH only $CuH_{-2}L^-$ and $CuH_{-1}L$ are present in the solution and have a 60:40 ratio. This solution was mixed by stopped-flow with a solution of the desired proton acceptor. The pH of the latter solution was at least 1.5 units higher than that of copper(II) triglycine. The rates were followed by observing the appearance of $CuH_{-2}L^-$ at 555 mμ.

Results

Reaction of $CuH_{-2}L^-$ with Acid. The rate of reaction of $CuH_{-2}L^-$ with EDTA in the pH region where monoprotonated EDTA is the predominant species had no dependence upon the EDTA concentration. However, in the pH region where a significant fraction of EDTA was diprotonated, the rate was responsive to the EDTA concentration. This behavior is not in agreement with EDTA acting as a nucleophile because $HEDTA^{3-}$ is more reactive than H_2EDTA^{2-},[14] but it does agree with H_2EDTA^{2-} acting as a better proton-transfer agent. The same behavior was observed for *trans*-1,2-diaminocyclohexanetetraacetate (CyDTA) which, because of steric requirements, cannot react readily by a nucleophilic mechanism. Other acids also catalyze the reaction and the mechanism is given in eq 2 and 3 where the reaction of the general acid (HX) in eq 2 is the rate-determining step.

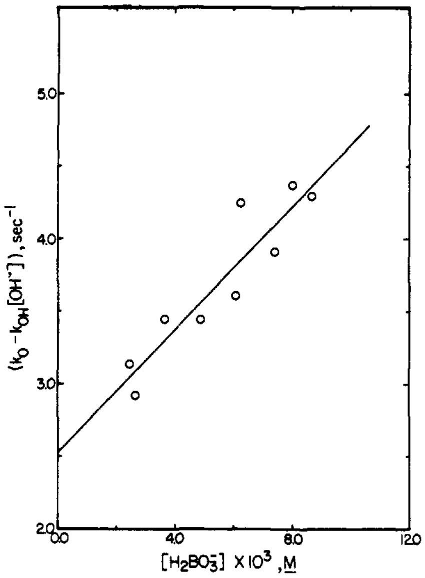

Figure 2. Effect of borate ion concentration on the rate constant $k_0 - k_{OH}[OH^-]$ for the reaction of base with $CuH_{-1}L$. The slope equals $k_{H_2BO_3}$ and the intercept equals k_{H_2O}.

$$CuH_{-2}L^- + HX \xrightarrow{k_{HX}} CuH_{-1}L + X^- \qquad (2)$$

$$CuH_{-1}L + HEDTA^{3-} + H^+ \xrightarrow{\text{fast}} CuEDTA^{2-} + HL \qquad (3)$$

The experimentally observed first-order rate constant, k_0, is the sum of the contributions of all the species to reaction 2.

$$k_0 = \sum_{HX} k_{HX}[HX] \qquad (4)$$

A summary of the k_{HX} values is given in Table I.

Table I. Rate Constants for Proton Transfer from General Acids to $CuH_{-2}L^-$ (25.0°, $\mu = 0.10\ M\ NaClO_4$)

General acid	k_{HX}, $M^{-1}\ sec^{-1}$	Log k_{HX}	pK_a	ref
H_2CyDTA^{2-}	4.4×10^3	3.64	6.12	*a*
H_2EDTA^{2-}	3.1×10^3	3.49	6.16	*a*
$H \cdot lutidine^+$	3.9×10^2	2.56	6.75	*b*
$H \cdot Tris^+$	17	1.22	8.10	*a*
H_3BO_3	2.2	0.35	9.00	*a*
H_3O^+	4.9×10^6	6.69	−1.74	
H_2O	3.2×10^{-5}	−4.5	15.52	

[a] L. G. Sillen and A. E. Martell, "Stability Constants of Metal-Ion Complexes," 2nd ed, The Chemical Society, London, 1964. [b] H. C. Brown and X. R. Mihm, *J. Am. Chem. Soc.*, **77**, 1723 (1955).

The dependence of the exchange rate of H_3O^+ is shown in Figure 1. These data were obtained by subtracting the H_2EDTA^{2-} and the buffer contri-

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[13] R. G. Bates, "Determination of pH," John Wiley and Sons, Inc., New York, N. Y., 1964, p 74.

[14] D. B. Rorabacher and D. W. Margerum, *Inorg. Chem.*, **3**, 382 (1964).

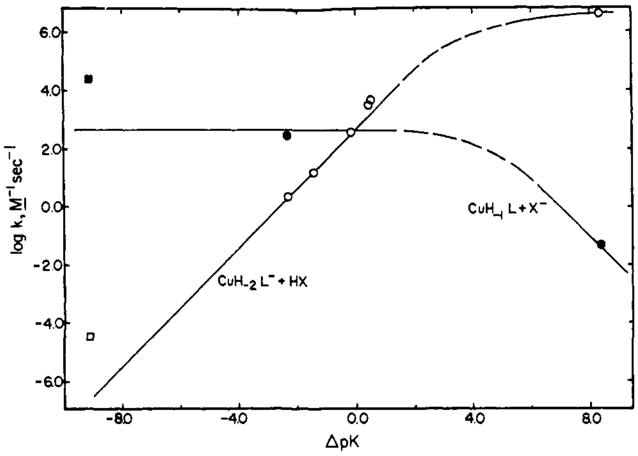

Figure 3. Proton-transfer rate constants as a function of Δp*K*. The points (○) for HX and $CuH_{-2}L^-$ are from left to right H_3BO_3, $H\cdot Tris^+$, $H\cdot lutidine^+$, H_2EDTA^{2-}, H_2CyDTA^{2-}, and H_3O^+. The points (●) for X^- with $CuH_{-1}L$ are from left to right $H_2BO_3^-$ and H_2O. The points along the solid curves are for the I ⇄ II ⇄ III ⇄ IV mechanism given in Figure 4. The points □ for H_2O + $CuH_{-2}L^-$ and ■ for OH^- + $CuH_{-1}L$ are for the I ⇄ V ⇄ IV mechanism and are not expected to be on the curve.

butions from the observed rate constant, eq 5. The solid line in Figure 1 was calculated from the rate

$$(k_H[H^+] + k_d) = k_0 - k_{H_2EDTA}[H_2EDTA^{2-}] - k_{H\cdot buffer}[H\cdot buffer] \quad (5)$$

constants (k_H and k_d) and the hydrogen ion concentration. The value[15] of k_H is 4.9×10^6 M^{-1} sec^{-1} and the k_d is 0.12 sec^{-1}. The constant k_d is attributed to a molecular rearrangement of $CuH_{-2}L^-$ to a form that can react directly with EDTA, the rate being limited by the rearrangement. It is possible that H_2O and $HEDTA^{3-}$ could contribute to k_d, but the predicted contributions from these species are all much less than k_d and believed to be insignificant.

Reaction of $CuH_{-1}L$ with Base. The rate of reaction of $CuH_{-1}L$ with $H_2BO_3^-$ to form $CuH_{-2}L^-$ is dependent upon the base concentration as shown in Figure 2. The slope is $k_{H_2BO_3}$ and equals $2.1 \pm 0.3 \times 10^2$ M^{-1} sec^{-1}. The value of the intercept, 2.5 ± 0.2 sec^{-1}, is the rate constant for the reaction of water with $CuH_{-1}L$ or as a second-order rate constant equals 4.5×10^{-2} M^{-1} sec^{-1}.

The rate constant for the reaction of $CuH_{-1}L$ with hydroxide ion also was determined by a pH-jump method. The hydroxide ion concentration was varied from 4.3×10^{-4} to 38×10^{-4} *M* and the k_{OH} value is 2.5×10^4 M^{-1} sec^{-1}. Rate constants for $CuH_{-1}L$ acting as an acid are listed in Table II.

Table II. Rate Constants for $CuH_{-1}L$ Acting as an Acid (25.0°, μ = 0.10 *M* $NaClO_4$)

Base, X^-	k_X, M^{-1} sec^{-1}
$H_2BO_3^-$	$2.1 \pm 0.3 \times 10^2$
OH^-	2.5×10^4
H_2O	$4.5 \pm 0.3 \times 10^{-2}$

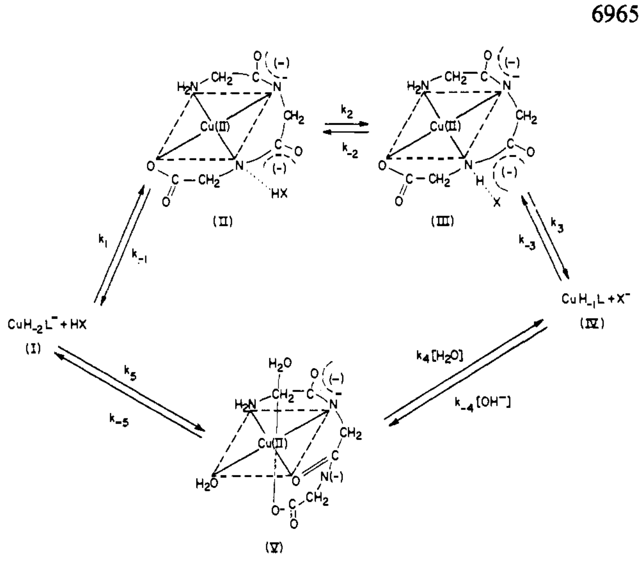

Figure 4. Proposed mechanism for the proton-transfer reactions of copper(II) triglycine.

Discussion

Mechanism of Acid Reaction with $CuH_{-2}L^-$. Log k_{HX} is plotted against Δp*K* ($pK_{acceptor} - pK_{donor}$) in Figure 3. The limiting value of k_{HX} for the reaction with H_3O^+ is four orders of magnitude less than the normal diffusion-controlled rates with hydrogen ion.[16] The slope, $\alpha = d(\log k_{HX})/d(\Delta pK)$, equals unity even when $\Delta pK = 0$, whereas in normal proton-transfer reactions $\alpha = 0.5$ in this region. The fact that $\alpha = 1$ indicates that the proton must be transferred from HX to $CuH_{-2}L^-$ before the rate-determining step. A mechanism is proposed in Figure 4. In this mechanism the proton is transferred to the peptide nitrogen rather than to the carbonyl oxygen of the peptide link because the latter transfer would tend to stabilize the enol form rather than give $CuH_{-1}L$. This pathway also has been shown to be unproductive in enol to keto reactions of acetylacetone[16] and diacetylacetone.[17] The peptide nitrogen next to the carboxylate group is assumed to be the point of attack. The carboxylate end of the complex is more labile and nuclear magnetic resonance studies with triglycine[18] have shown that the peptide nitrogen nearest to the carboxylate group is the most basic.

In Figure 4 the path I → II → III → IV is proposed for acids with the exception of water where V is believed to be an intermediate as discussed in the next section.

The forward rate constant for HX can be expressed by eq 6 and the reverse rate constant, k_X, by eq 7.

$$k_{HX} = \frac{k_1k_2k_3}{k_{-1}k_{-2} + k_{-1}k_3 + k_2k_3} \quad (6)$$

$$k_X = \frac{k_{-1}k_{-2}k_{-3}}{k_{-1}k_{-2} + k_{-1}k_3 + k_2k_3} \quad (7)$$

For both reactions stationary-state conditions are applied to intermediates II and III. These two rate constants, k_{HX} and k_X, can be simplified because the equilibrium between II and III lies to the left. The nitrogen atom in structure II is a very weak base and

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[15] In ref 11 we reported the value for k_H to be 6.6×10^6 M^{-1} sec^{-1}. However, this was based on pH measurements and the more correct value is 4.9×10^6 M^{-1} sec^{-1} based on hydrogen ion concentrations.

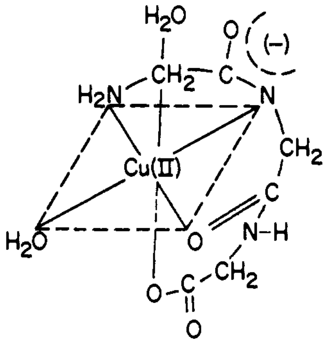
[16] M. Eigen, *Angew. Chem.*, **75**, 489 (1963). The present work follows the theoretical treatment given in this reference.

[17] J. Stuehr, *J. Am. Chem. Soc.*, **89**, 2826 (1967).

[18] M. Sheinblatt, *ibid.*, **88**, 2123 (1966).

there are no major changes in configuration in structure III so that $k_{-2} \gg k_2$ except for H_3O^+. There are major electronic and structural rearrangements between III and IV; thus $k_{-2} \gg k_3$ and $k_{-1} \gg k_3$ and eq 6 and 7 reduce to $k_{HX} = K_1K_2k_3$ and $k_X = k_{-3}$, respectively. This is consistent with the data shown in Figure 3 where $\alpha = 1$ and $\beta = 0$ in the region of $\Delta pK = 0$ ($\beta = d(\log k_X)/d(\Delta pK)$ and $\alpha + \beta = 1$). A β value of zero often implies that the reverse rate is diffusion controlled, but this is not necessary for the $CuH_{-1}L$ reaction with X^- because k_{-1} and k_{-2} are much greater than k_{-3}.

The rate of formation of II should be diffusion controlled so that k_1 is large. Although step II → III must change the peptide nitrogen to a tetrahedral configuration, this reaction should be fast compared to the rearrangement in step III → IV. Reactions II → III could be faster than the corresponding reaction of the enol form of acetylacetonate ion because nitrogen is capable of hydrogen-bonding. The reaction of H_3O^+ with acetylacetonate has a rate constant of 1.2×10^7 M^{-1} sec^{-1} at 12°.[16] The kinetics of hydroxide ion reaction with $CuH_{-1}L$ necessitate a structure for $CuH_{-1}L$ which differs from III. The structure proposed is shown in IV which agrees with coordination of the carbonyl oxygen found in crystals. Therefore the transition from III to IV involves dissociation and rearrangement of copper–ligand bonds. Changing the metal from copper to nickel causes a decrease in the values of k_{HX} despite a more favorable ΔpK and is consistent with the proposed type of change in coordination.[19]



IV ($CuH_{-1}L$)

It has been pointed out that an equilibrium preceding proton transfer can account for rates that are less than diffusion controlled.[16,20] However, a prior dissociation of the $-N^-$- group from copper followed by proton transfer can be ruled out. The imide group would be a very strong base, and its reaction with HX would not depend on the acidity of HX. Hence α would approach zero rather than the value of 1 found in this work.

The effect of ΔpK on k_{HX} is largely associated with K_2 $(= k_2/k_{-2})$ while the values for K_1 $(= k_1/k_{-1})$ should be similar to values for outer-sphere complexes. From the electrostatic attraction with the $CuH_{-2}L^-$ the acids $H\cdot lutidine^+$ and $H\cdot Tris^+$ should have larger K_1 values than H_2EDTA^{2-} and H_2CyDTA^{2-}. However, the k_{HX} values for H_2EDTA^{2-} and H_2CyDTA^{2-} fall above the line of $\alpha = 1$ in Figure 3 indicating that if k_3 is constant the carboxylate groups of EDTA or CyDTA are weakly bonded to the axial position of copper in $CuH_{-2}L^-$. Apical interaction with copper(II) complexes has been reported.[21]

Mechanism of Base Reactions with $CuH_{-1}L$. When ΔpK is zero k_{HX} must equal k_X. In addition the sum of the slopes α and β must equal unity so the curve for the base reaction with $CuH_{-1}L$ can be constructed from the value of k_{HX} at $\Delta pK = 0$ and the H_2O rate constant taken from Table II. The reaction of $H_2BO_3^-$ with $CuH_{-1}L$ gives a rate constant of 210 M^{-1} sec^{-1} in agreement with the constructed curve with $k = 500$ when $\beta = 0$. A somewhat unique situation exists in that the reaction between $H_2BO_3^-$ and $CuH_{-1}L$, and the reaction between H_3BO_3 and $CuH_{-2}L^-$ could each be measured independently. This is the case because the latter reaction was driven by the subsequent reaction with EDTA. The β curve in Figure 3 corresponds to the IV → III → II → I path and the rate-determining step is k_{-3}.

The ratio of k_{HX}/k_X agrees within a factor of 2 with the equilibrium ratio of $K_{a(HX)}/K_{a(CuH_{-1}L)}$ for H_3O^+ and for H_3BO_3.

The reaction of $CuH_{-1}L$ with hydroxide ion is too fast by a factor of 50 to be accounted for by path IV → III → II → I, and the IV → V → I mechanism in Figure 4 is proposed. Cooper(II)-catalyzed ester hydrolysis proceeds through an activated intermediate which has the carbonyl oxygen coordinated to the metal.[22] A similar intermediate is proposed for the hydroxide ion reaction. Coordination of the carbonyl group would labilize the hydrogen atom bonded to the peptide nitrogen, thus facilitating the removal of the proton before copper is coordinated to the imide nitrogen. Applying the steady-state condition to species V gives

$$k_{OH} = \frac{k_{-4}k_{-5}}{k_4 + k_{-5}} = 2.5 \times 10^4\ M^{-1}\ \text{sec}^{-1} \qquad (8)$$

The extent to which copper coordination to the carbonyl group labilizes the peptide proton cannot be definitely assigned, but the pK_a must be quite large. Hydroxide ion apparently is a strong enough base, with the aid of copper coordination, to extract the proton from the peptide link to form structure V. Other bases will have a much smaller ratio of k_{-4}/k_4 and therefore will not react by this path.

The value of k_{-4} should approach the diffusion-controlled limit of 10^{10} M^{-1} sec^{-1} because there is little rearrangement between structures IV and V. Under these circumstances quite weak acids ($pK = 11$–12) still react at the diffusion limit. It can be seen from eq 8 that in order for $k_{-4} \gg 10^4$ M^{-1} sec^{-1}, k_4 must be much larger than k_{-5}. Equation 9 follows therefore

$$k_5 = \left(\frac{k_{-4}k_{-5}}{k_4}\right)\left(\frac{K_w}{K_a}\right) = 1.8 \times 10^{-3}\ \text{sec}^{-1} \qquad (9)$$

from the equilibrium constant of IV and I. The value for k_{H_2O} in Table I and in Figure 3 is $k_5/55.5$ M^{-1} sec^{-1}. This point falls above the α slope of unity because it is for the I → V → IV mechanism rather than the I → II → III → IV mechanism.

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[19] E. J. Billo and D. W. Margerum, submitted for publication.

[20] J. N. Brønsted and K. Pedersen, *Z. Physik. Chem.*, **108**, 185 (1923).

[21] K. M. Wellman, T. G. Mecca, W. Mungall, and C. R. Hare, *J. Am. Chem. Soc.*, **90**, 805 (1968).

[22] M. L. Bender and B. W. Turnquest, *ibid.*, **79**, 1889 (1957).

Conclusions

The proton-transfer reactions

$$CuH_{-2}L^- + H_3O^+ \longrightarrow CuH_{-1}L + H_2O$$
$$CuH_{-1}L + OH^- \longrightarrow CuH_{-2}L^- + H_2O$$

are many orders of magnitude slower than the usual diffusion-controlled rate constants for reactions with H_3O^+ and OH^-. The reactions of different acids and bases with copper(II) triglycine fit the theoretical kinetic behavior outlined by Eigen[16] which relates the rate constants to ΔpK values. The limiting rate step in these reactions does not result from diffusion but rather from the necessity to break and rearrange coordinate bonds to copper.

Two reaction paths are proposed for the proton transfer, one which ought to be encountered for most acids and bases ($I \rightleftarrows II \rightleftarrows III \rightleftarrows IV$) and another ($I \rightleftarrows V \rightleftarrows IV$) which is limited to the reaction of very strong bases (near the base strength of OH^-) with $CuH_{-1}L$ or to the reaction of very weak acids (near the acid strength of H_2O) with $CuH_{-2}L^-$.

The copper-imide bond in $CuH_{-2}L^-$ is not easily broken, and the preferred dissociation occurs after the addition of a proton to the peptide nitrogen. Thus, EDTA does not react as a nucleophilic group with $CuH_{-2}L^-$ but rather as the acid H_2EDTA^{2-}, just furnishing a proton to give more labile coordination which permits rearrangement to a copper-triglycine complex more sterically favorable for EDTA coordination. Other ligands, less sterically hindered, can react as nucleophiles with $CuH_{-2}L^-$.[23]

Acknowledgment. This investigation was supported by Public Health Service Research Grant No. GM-12152 from the National Institute of General Medical Science.

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[23] (a) G. K. Pagenkopf and D. W. Margerum, *J. Am. Chem. Soc.*, **90**, 502 (1968); (b) submitted for publication.

Ligand Penetration Rates into Metal Ion Coordination Spheres. Aluminum(III), Gallium(III), and Indium(III) Sulfates

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Contribution from the Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106. *Received June 17, 1968*

Abstract: Kinetics of the sulfate ion complexing with Al(III), Ga(III), and In(III) have been measured by the pressure-jump and temperature-jump techniques. The measurements were carried out in acid solutions (pH 1–3) in order to minimize hydrolysis and polymerization. For each system a single relaxation time was observed; moreover, for each system the inverse relaxation time could be interpreted only as the sum of two parallel pathways, one with sulfate reacting with the solvated metal ion and the other with sulfate reacting with the monohydroxy metal ion. The zero ionic strength forward rate constants for Al(III), Ga(III), and In(III) are 1.2×10^3, 2.1×10^4, and 2.6×10^5 M^{-1} sec^{-1} for the direct reaction and 8.5×10^5, 1.0×10^5, and 2.5×10^7 M^{-1} sec^{-1} for the monohydroxy route, respectively. These results were consistent with the Eigen–Tamm mechanism for the stepwise formation of metal complexes. The first-order ligand penetration rate constants were estimated to be 1, 20, and 300 sec^{-1} for the three ions. That for Al(III) is in excellent agreement with the water lifetime as recently measured by nmr. The value for Ga(III) is substantially less than the water exchange rate. As a result, it is concluded that sulfate penetration into the primary coordination sphere of the metal ion proceeds *via* a largely SN1 mechanism for Al and primarily by an SN2 mechanism for Ga; In also appears to be SN2.

The development of relaxation techniques[2] has permitted the investigation of very rapid chemical processes whose half-lives are between several seconds and 10^{-10} sec. A particularly large amount of data is now available for elementary steps in metal complexing reactions.[3,4] To date, experimental studies have been largely confined to the alkali, alkaline earth, and the divalent first-row transition metal ions. Relatively few experimental studies of rapidly reacting trivalent metal ion systems have been undertaken, presumably because such ions are subject to complications due to hydrolysis and polymerization. It is the purpose of this investigation to kinetically characterize three such systems: aqueous Al(III), Ga(III), and In(III).

Eigen[5] lists the characteristic rate constants for water displacement in the inner coordination sphere as 10^0–10^1 and $10^{1.5}$–$10^{2.5}$ sec^{-1} for gallium and indium, respectively. These were obtained apparently from the extrapolation of rate data for other charge types. Geier[6] conducted a kinetic study of the complexing of several trivalent metal ions, including In^{3+}, with murexide.

Experimental Section

Materials. All metals were obtained as the sulfates (99.9%) from Rare and Fine Chemicals Inc. A small amount of each salt

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