found in $PdCl_2$[22] but similar to the average Pt–Cl distance of 2.37 (1) Å found[5] for the ethanol adduct of a platinum (II) isocyanide complex.

The C–N and N–N bond distances of the chelate ring indicate some multiple-bond character for these bonds and are similar to the distances found in diformylhydrazine[23] and diacetylhydrazine.[24] The C–N distances are 1.325 (4) and 1.341 (8) Å in these compounds, whereas the C_2–N_2 distance here is 1.309 (6) Å; the N–N distance of 1.395 (8) Å found here is identical with 1.392 (7)[23] and 1.396 (9) Å[24] in the hydrazine derivatives. The N–N distance in hydrazine is 1.46 Å.[25]

The C_2–N_1 distance of 1.327 (7) Å is not significantly different from the C_2–N_2 distance and indicates multiple-bond character for the C–N bond external to the ring. This distance also implies that there will be a large barrier to rotation about the C_2–N_1 bond and that cis–trans isomerism about this bond might be observed under certain conditions. Indeed, in the closely related complex resulting from the addition of methylhydrazine to $Pt(CNCH_3)_4^{2+}$ both isomers occur in the same molecule.[26]

A projection of the structure along c is shown in Figure 2. The molecular plane of the complex is normal to the c axis of the crystal, and the molecules are stacked to form infinite chains parallel to c. The interplanar distance is $c/2$ (3.420 Å) and the Pd···Pd distance is 3.606 Å.

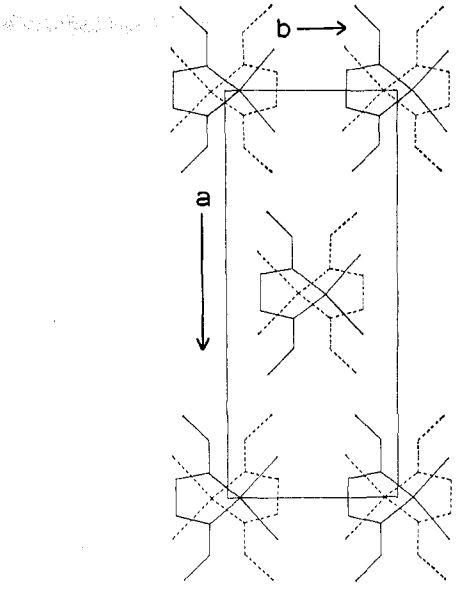

Figure 2.—The crystal structure of $[(CH_3)_2C_2N_4H_4]PdCl_2$ projected along the c axis.

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Triglycine Autocatalysis of the Reaction between Copper–Triglycine and Ethylenediaminetetraacetate Ion

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The reaction between copper–triglycine ($CuH_{-2}L^-$) and EDTA is catalyzed by the released triglycinate ion (L^-). This autocatalysis reaction is shown to proceed *via* the bis-triglycine complex, $CuH_{-2}L_2^{2-}$, which is attacked more readily by $EDTA^{4-}$ than is the mono complex, $CuH_{-2}L^-$. Steric hindrance prevents EDTA from being an effective nucleophile with the mono complex and the postulated role of the second triglycine in the autocatalysis process is to facilitate the formation of a complex with only one Cu–N(peptide) bond. The bis complex is more readily converted to such a form than is the mono complex and this form does not sterically hinder nitrogen coordination by EDTA to a planar copper site. The detailed kinetic dependence of L^-, OH^-, and $EDTA^{4-}$ is accounted for including the appearance of rate maxima as a function of pH and L^- concentration and limiting rates at high EDTA concentrations.

Introduction

The transfer of copper ion from the copper(II)–triglycine complex to ethylenediaminetetraacetate ion is catalyzed by the released triglycine in solutions above pH 8. The exchange reaction is given in eq 1 where L^- is the glycylglycylglycinate ion and $CuH_{-2}L^-$ is the complex in which two protons are ionized from the peptide nitrogens. EDTA is a poor nucleophile in its reaction with $CuH_{-2}L^-$ and the manner in which a second triglycinate ion activates the transfer of copper to EDTA is of interest. Steric factors are important in controlling which ligands are able to react as nucleophiles with $CuH_{-2}L^-$, and EDTA, as well as other ligands with only tertiary nitrogens, is sterically hin-

$$CuH_{-2}L^- + \begin{bmatrix} EDTA^{4-} + 2H_2O \\ \uparrow\downarrow \\ HEDTA^{3-} + H_2O \end{bmatrix} \longrightarrow \begin{bmatrix} 2OH^- \\ \\ OH^- \end{bmatrix} + CuEDTA^{2-} + L^- \quad (1)$$

dered.[1] Nevertheless, the path of autocatalysis observed for the reaction is the formation of a bis-triglycine complex and its attack by EDTA.

Below pH 8 the reaction has little or no L^- catalysis and was found to depend upon either a first-order rearrangement of $CuH_{-2}L^-$ or proton transfers from general acids (HX) such that the rate equals $(k_d + k_{HX}[HX])[CuH_{-2}L^-]$.[2] The general acids include H_3O^+, H_2EDTA^{2-}, and acid forms of buffers. The rate constant for the molecular rearrangement (k_d) does not vary with pH and therefore this pathway contributes to the rate above pH 8. Under the conditions used in the present study the general acid catalysis path does not contribute significantly to the observed reaction rates. On the other hand, the catalysis by L^- in eq 1 is very important.

Experimental Section

Kinetic runs were performed using a Durrum–Gibson stopped-flow spectrophotometer with a 2.0-cm cell path. The photomultiplier output was interfaced to a Hewlett-Packard 2115A general-purpose digital computer as described elsewhere.[3] Using this system, up to 250 data points may be taken at a rate as fast as 1 point/msec. A least-squares analysis of the conformance of the data to a programmed rate law is performed on line. After on-line analysis, data from all stopped-flow experiments were recorded on punched paper tape for possible later off-line calculations.

The reaction between copper–triglycine and EDTA was followed by the disappearance of $CuH_{-2}L^-$ which has a higher molar absorptivity than $CuEDTA^{2-}$ at 235 nm (4650 *vs.* 3650, respectively). Each rate constant is the average of at least four kinetic runs and is listed with its standard deviation.

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. Diethylenetriaminepentaacetic acid was obtained from the J. T. Baker Chemical Co. and recrystallized from water as the free acid. A 0.0920 *M* stock solution was prepared and standardized by the mole ratio method with copper(II). The copper–triglycine solutions were freshly prepared before each series of reactions. Ionic strength was maintained at 0.10 *M* with $NaClO_4$. Hydrogen ion concentrations were calculated from pH measurements using $-\log [H^+] = pH - 0.11$,[4] and hydroxide ion concentrations were calculated from $pK_w = 13.78$. Sodium tetraborate was used as the buffering agent (total borate 5.0×10^{-3} *M*). The protonation constants for the ligands used in this study are as follows: HL, $pK_a = 7.88$;[5] $H(EDTA)^{3-}$, $pK_a = 10.26$;[6] $H(DTPA)^{4-}$, $pK_a = 10.42$;[6] $H_2(DTPA)^{3-}$, $pK_a = 8.76$.[6] All of the above were determined at an ionic strength of 0.1 at 25.0° with the exception of $H(EDTA)^{3-}$ which was determined at 20.0°.

Results

The rate of the exchange reaction in eq 1 depends upon the pH and upon the concentrations of the complex, of triglycine, and of EDTA, but the dependence is complicated. The major facts are as follows. (1) The reaction is first order in $[CuH_{-2}L^-]$ under all conditions. (2) The L^- catalysis increases from pH 8 to 9.7 and in this pH range there is little or no EDTA dependence (Table I, section A). (3) Above pH 9.7 the rate decreases with pH and becomes dependent upon EDTA (Table I, section B). (4) The rate reaches a limiting value at high $EDTA^{4-}$ concentrations (Table I, section C). (5) Above pH 9.7 the rate increases with increasing triglycine concentration but reaches a maximum and then decreases as the triglycine concentration is further increased (Table I, section D). (6) Above pH 11.5 the contributions from k_d and a direct reaction of $EDTA^{4-}$ with $CuH_{-2}L^-$ become more important than the autocatalytic path (Table I, section E). (7) At low pH a slight dependence in $H(EDTA)^{3-}$ is found with $H(EDTA)^{3-}$ in great excess and free triglycine in only trace amounts (Table I, section F).

TABLE I

EFFECT OF TRIGLYCINE AND EDTA CONCENTRATIONS ON THE RATE OF THE EXCHANGE REACTION BETWEEN $CuH_{-2}L^-$ AND EDTA ($[CuH_{-2}L^-]_T = 3.95 \times 10^{-5}$ *M*, $\mu = 0.10$ ($NaClO_4$), 25.0 ± 0.1°)

$10^3[L^-]_{excess}$, *M*	$10^4[EDTA]_T$, *M*	pH	k_{obsd}, sec^{-1}
	A. pH below 9.7		
0.50	2.00	8.8	0.174 ± 0.001
1.00	2.00	8.8	0.225 ± 0.002
1.50	2.00	8.8	0.312 ± 0.004
2.00	2.00	8.8	0.351 ± 0.006
0.50	2.00	9.2	0.232 ± 0.001
1.00	2.00	9.2	0.455 ± 0.006
1.50	2.00	9.2	0.508 ± 0.009
2.00	2.00	9.2	0.634 ± 0.007
1.00	1.00	9.09	0.29 ± 0.01[a]
1.00	2.00	9.03	0.24 ± 0.01[a]
1.00	3.00	9.07	0.27 ± 0.01[a]
1.00	4.00	9.07	0.27 ± 0.01[a]
	B. EDTA Dependence above pH 9.7		
1.00	1.00	10.85	0.30 ± 0.01[a]
1.00	2.00	10.92	0.59 ± 0.07[a]
1.00	3.00	10.89	0.73 ± 0.03[a]
1.00	4.00	10.87	0.93 ± 0.06[a]
	C. Limiting Rate at High $EDTA^{4-}$ Concentration		
90.0	41.2	9.77	12.1 ± 0.2
90.0	82.4	9.77	14.1 ± 0.3
90.0	124	9.81	14.9 ± 0.1
90.0	206	9.94	15.0 ± 0.2
90.0	270	9.94	15.5 ± 0.7
	D. Triglycine Dependence above pH 9.7		
0.50	2.00	10.65	0.66 ± 0.03
1.00	2.00	10.70	0.91 ± 0.03
1.50	2.00	10.65	1.03 ± 0.02
2.00	2.00	10.65	1.20 ± 0.01
2.50	2.00	10.65	1.20 ± 0.03
4.00	2.00	10.62	1.03 ± 0.03
6.00	2.00	10.64	0.95 ± 0.06
8.00	2.00	10.63	0.82 ± 0.03
10.0	2.00	10.68	0.74 ± 0.02
	E. $EDTA^{4-}$ Dependence at High pH		
1.00	2.00	11.60	0.265 ± 0.006
0.04	1.00	11.58	0.164 ± 0.008
0.04	2.00	11.58	0.284 ± 0.019
0.04	3.00	11.58	0.350 ± 0.007
0.04	4.00	11.61	0.376 ± 0.006
0.04	6.00	11.58	0.492 ± 0.008
0.04	8.00	11.59	0.611 ± 0.012
	F. $H(EDTA)^{3-}$ Dependence at pH ≃9		
0.005	2.00	8.92	0.132 ± 0.001
0.005	5.00	8.93	0.126 ± 0.003
0.005	10.0	8.95	0.187 ± 0.004
0.005	41.3	8.95	0.212 ± 0.016
0.005	103	8.96	0.28 ± 0.03
0.005	206	9.00	0.440 ± 0.015
0.005	310	9.00	0.57 ± 0.02

[a] These rate constants were calculated from data stored on Polaroid film.

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Typical autocatalytic kinetics are observed when reaction 1 is studied without excess triglycine as seen in Figure 1. In order to establish the mechanism the

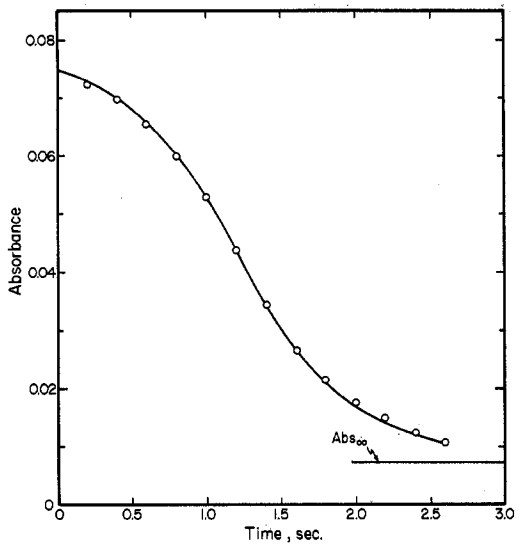

Figure 1.—Autocatalytic behavior of the exchange reaction between $CuH_{-2}L^-$ and EDTA with no excess triglycine present. $[CuH_{-2}L^-]_T = 1.97 \times 10^{-3}$ *M*, [EDTA] = 2.50×10^{-3} *M*, pH 10.0, 25.0°, μ = 0.1 ($NaClO_4$), λ 555 nm, cell path 0.2 cm.

reaction is studied by stopped-flow mixing of $CuH_{-2}L^-$ solutions with a mixture of excess triglycine and EDTA, so that the concentrations of L^- and EDTA are essentially constant during the reaction. First-order kinetics are observed with the rate equal to $k_{obsd}[CuH_{-2}L^-]$. Figure 2 shows the pH dependence of k_{obsd} when

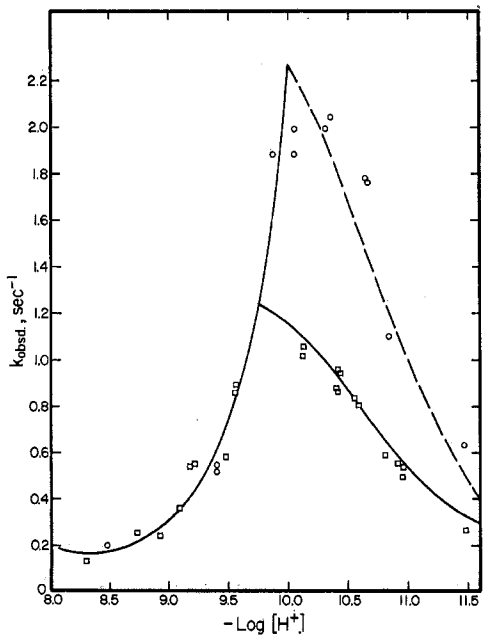

Figure 2.—Effect of pH on the observed rate constant for the triglycine-catalyzed reaction of $CuH_{-2}L^-$ with EDTA. $[CuH_{-2}L^-]_T = 3.95 \times 10^{-5}$ *M*, $[L^-]_{excess} = 1.00 \times 10^{-3}$ *M*, $[EDTA]_T = 2.00 \times 10^{-4}$ *M*, [boric acid–borate buffer] = 5.0×10^{-3} *M*, 25.0°, μ = 0.10 ($NaClO_4$). The points are experimental. The portion of the solid line where k_{obsd} is increasing with pH is calculated from k_d, k_1, and k_{HX} (HX = H_3O^+, H_2EDTA^{2-}, and H_3BO_3). The portion of the solid line where k_{obsd} is decreasing with pH is calculated from k_d, k_2, k_3/k_{-2}, k_{-3}/k_4, and k_5: □, EDTA; ○, DTPA.

$[L^-] = 10^{-3}$ *M* and [EDTA] = 2×10^{-4} *M*. Below pH 9.7 $k_{obsd} = k_d + k_1[L^-][OH^-]$. Table I, section A, shows the increase in k_{obsd} as $[L^-]$ increases at pH 8.8 and at pH 9.2. In this pH region the k_{obsd} value is independent of the EDTA concentration as seen from the data at pH 9.03–9.09 in Table I, section A. The value of k_1 has been determined by independent kinetic studies of the mono- and bis(triglycinato)cuprate(II) equilibrium and is 1.26×10^7 M^{-2} sec^{-1}.[7]

Above pH 9.7 the rate of formation of the bis complex ($CuH_{-2}L_2^{2-}$) becomes so fast that later steps in the reaction sequence are rate determining. The proposed mechanism is given in eq 2–5. The initial hydroxide acceleration followed by hydroxide inhibition is seen in Figure 2.

$$CuH_{-2}L^- + L^- + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CuH_{-2}L_2^{2-} + OH^- \quad (2)$$

$$CuH_{-2}L_2^{2-} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} CuH_{-1}L_2^- + OH^- \quad (3)$$

$$CuH_{-1}L_2^- + EDTA^{4-} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} Cu(H_{-1}L)EDTA^{4-} + L^- \quad (4)$$

$$Cu(H_{-1}L)EDTA^{4-} \xrightarrow{k_4} CuEDTA^{2-} + L^- + OH^- \quad (5)$$

Above pH 11.5, hydroxide ion so severely inhibits the reaction sequence in eq 2–5 that triglycine catalysis becomes a minor contributor to the observed rate. In this region the rate is due largely to a combination of the k_d path (k_d = 0.12 sec^{-1})[2] and the direct attack of $EDTA^{4-}$ on $CuH_{-2}L^-$ (k_5 = 600 M^{-1} sec^{-1}) (data in Table I, section E). In earlier work[1] nucleophilic reactions were not observed with EDTA at pH 8–9 because $H(EDTA)^{3-}$ is an even poorer nucleophile than $EDTA^{4-}$. Studies of the direct rate of $H(EDTA)^{3-}$ attack on $CuH_{-2}L^-$ yield a rate constant (15 M^{-1} sec^{-1}) which is $^1/_{40}$th that of $EDTA^{4-}$ and is very sensitive to autocatalysis by triglycine (the $H(EDTA)^{3-}$ rate constant is determined from data in Table I, section F).

The mechanism given in eq 2–5 accounts for the dramatic increase and subsequent decrease of the rate of the triglycine-catalyzed reaction as a function of pH. It also accounts for the other major facts which have been outlined. In order to determine the relative contributions of eq 3–5 to the observed kinetic behavior above pH 9.7, eq 6 may be derived by assuming that $CuH_{-2}L_2^{2-}$ is present in equilibrium concentrations ($K_1 = k_1/k_{-1}$ = 175 M^{-1})[7] and applying stationary-state conditions to the concentrations of $CuH_{-1}L_2^-$ and $Cu(H_{-1}L)EDTA^{4-}$. The experimentally observed first-order rate constant (k_{obsd}) is corrected in eq 6 for

$$k'_{obsd} = \frac{k_2k_3k_4[EDTA^{4-}]\left(\frac{K_1[L^-]}{1 + K_1[L^-]}\right)}{k_{-2}k_{-3}[L^-][OH^-] + k_{-2}k_4[OH^-] + k_3k_4[EDTA^{4-}]} \quad (6)$$

the k_d and k_5 paths and for the degree to which $CuH_{-2}L_2^{2-}$ is formed (eq 7). For data obtained under

$$k'_{obsd} = k_{obsd} - (k_d + k_5[EDTA^{4-}])\frac{1}{1 + K_1[L^-]} \quad (7)$$

conditions of constant triglycine concentration (see Table II) eq 6 may be rearranged to yield eq 8, where $A = k_{-2}k_{-3}[L^-] + k_{-2}k_4$, $B = k_2k_3k_4K_1[L^-]/(1 +$

(7) G. R. Dukes and D. W. Margerum, submitted for publication.

TABLE II

DEPENDENCE OF k_{obsd} ON pH AT CONSTANT TRIGLYCINE CONCENTRATION ($[CuH_{-2}L^-]_T = 3.95 \times 10^{-5}$ *M*, $[L^-]_{excess} = 1.00 \times 10^{-3}$ *M*, $[EDTA]_T = 2.00 \times 10^{-4}$ *M*, $\mu = 0.10$ ($NaClO_4$), 25.0 ± 0.1°)

−log [H⁺]	k_{obsd}, sec⁻¹	−log [H⁺]	k_{obsd}, sec⁻¹	−log [H⁺]	k_{obsd}, sec⁻¹
10.12	1.02 ± 0.04	10.42	0.94 ± 0.02	10.91	0.55 ± 0.03
10.13	1.06 ± 0.03	10.56	0.84 ± 0.02	10.95	0.50 ± 0.06
10.40	0.88 ± 0.07	10.59	0.80 ± 0.03	10.96	0.54 ± 0.05
10.41	0.96 ± 0.05	10.81	0.59 ± 0.03	11.48	0.265 ± 0.006
10.41	0.87 ± 0.03				

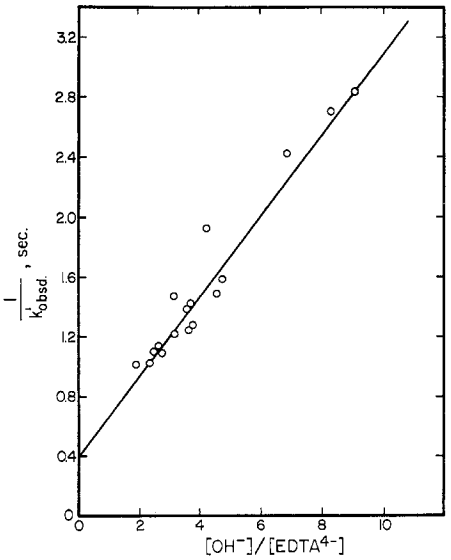

Figure 3.—Determination of k_2 for the reaction of $CuH_{-2}L^-$ with EDTA. The points are experimental and the solid line is a linear least-squares fit to the data.

$K_1[L^-]$), and $C = k_3k_4$. Figure 3 is a plot of $1/k'_{obsd}$

$$\frac{1}{k'_{obsd}} = \frac{A}{B}\frac{[OH^-]}{[EDTA^{4-}]} + \frac{C}{B} \quad (8)$$

vs. $[OH^-]/[EDTA^{4-}]$. From the intercept of Figure 3 (0.40) a value of 16.7 sec^{-1} is calculated for k_2, which agrees well with the limiting rate found at high $EDTA^{4-}$ concentrations. In a similar manner, for data obtained under conditions of constant pH and $EDTA^{4-}$ concentration, eq 6 may be rearranged to the form of eq 9, where $D = k_{-2}k_{-3}[OH^-]$, $E = k_2k_3k_4 \cdot [EDTA^{4-}]$, and $F = k_{-2}k_4[OH^-] + k_3k_4[EDTA^{4-}]$.

$$\frac{1}{k'_{obsd}}\left(\frac{K_1[L^-]}{1 + K_1[L^-]}\right) = \frac{D[L^-]}{E} + \frac{F}{E} \quad (9)$$

Figure 4 is a plot of $1/k'_{obsd}(K_1[L^-]/(1 + K_1[L^-]))$ *vs.* $[L^-]$ (see Table I, section D for data). From the slope and intercept of Figure 4 (slope = 83.7 sec M^{-1} and intercept = 0.115 sec) and the value of k_2 determined from Figure 3 (16.7 sec^{-1}) the ratios of k_3/k_{-2} and k_{-3}/k_4 may be determined. The calculated value of k_3/k_{-2} is 4.76 and $k_{-3}/k_4 = 1.52 \times 10^3\ M^{-1}$.

Discussion

The rate constants evaluated or used in this study are given in Table III. The contributions from the three acid reactants ($H_2(EDTA)^{2-}$, H_3BO_3, and H_3O^+) are negligible for most of the conditions used. However, these constants account for the slight upturn in the calculated curve near pH 8 in Figure 2. In previous work[2] the general acid (HX) catalytic pathway was established for the reaction of $CuH_{-2}L^-$ with HX in the presence of EDTA. The value of k_{HX} was shown to be directly dependent upon the acidity constant of

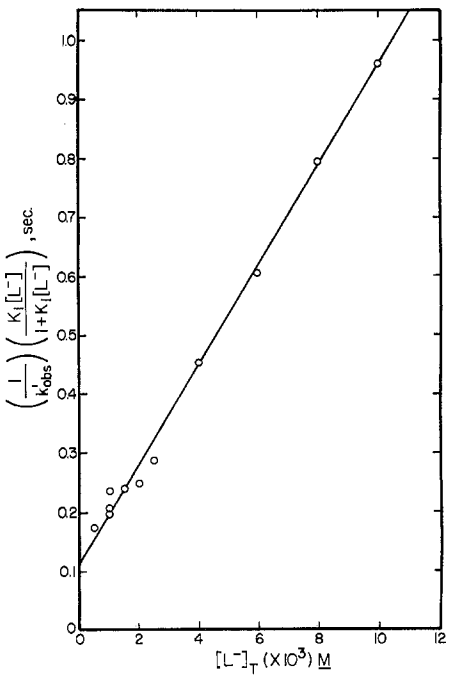

Figure 4.—Determination of k_3/k_{-2} and k_{-3}/k_4 for the reaction of $CuH_{-2}L^-$ with EDTA. The points are experimental and the solid line is a linear least-squares fit to the data.

TABLE III

RATE CONSTANTS EVALUATED OR USED IN THIS STUDY (25.0°, $\mu = 0.10$ ($NaClO_4$))

For Reactions in Basic Solution	
k_d	0.12 sec^{-1}
k_1	$1.26 \times 10^7\ M^{-2}\ sec^{-1}$
k_{-1}	$8.79 \times 10^4\ M^{-1}\ sec^{-1}$
k_2	16.7 sec^{-1}
k_3/k_{-2}	4.76
k_{-3}/k_4	$1.52 \times 10^3\ M^{-1}$
$EDTA^{4-} + CuH_{-2}L^-$ (k_5)	$6.0 \times 10^2\ M^{-1}\ sec^{-1}$
$H(EDTA)^{3-} + CuH_{-2}L^-$	$15\ M^{-1}\ sec^{-1}$
For Acid Reactants	
$H_2(EDTA)^{2-} + CuH_{-2}L^-$	$3.1 \times 10^3\ M^{-1}\ sec^{-1}$
$H_3BO_3 + CuH_{-2}L^-$	$2.2\ M^{-1}\ sec^{-1}$
$H_3O^+ + CuH_{-2}L^-$	$4.9 \times 10^6\ M^{-1}\ sec^{-1}$

HX. Hence, the kinetic contributions of HL and of $H(EDTA)^{3-}$ as general acids can be calculated and shown to be insignificant under the conditions used. No rate dependence was found for HL and the high pK_a value for $H(EDTA)^{3-}$ indicates that it cannot be acting as an acid with $CuH_{-2}L^-$ but must be reacting as a nucleophile as in the case for L^- and for $EDTA^{4-}$.

The nucleophilic reactivity of $H(EDTA)^{3-}$ and of $EDTA^{4-}$ with $CuH_{-2}L^-$ is much less than for diamines or polyamines (which have rate constants of about 10^7 $M^{-1}\ sec^{-1}$) or for ethylenediaminediacetate (EDDA) ($k_{obsd} = 3.6 \times 10^4\ M^{-1}\ sec^{-1}$ at pH 8.4).[1] In the case

of the nickel complex it has been shown[8] that aminocarboxylate chelates are less effective than diamines but that they do react with $NiH_{-2}L^-$. Furthermore, even aminocarboxylates which contain only tertiary nitrogens can react if one of the carboxylate groups is not sterically blocked from entering a planar coordination site (in the plane of the metal and the nitrogen atoms of triglycine). This mode of reaction is proposed for $CuH_{-2}L^-$ and $EDTA^{4-}$ ($k_5 = 600\ M^{-1}\ sec^{-1}$) *via* an in-plane coordination of one of the $EDTA^{4-}$ carboxylate groups. Therefore, steric factors (the two tertiary nitrogens in EDTA *vs.* the two secondary nitrogens in EDDA) and to a lesser extent electrostatic factors make $EDTA^{4-}$ a relatively ineffective nucleophile with $CuH_{-2}L^-$. $H(EDTA)^{3-}$ ($k = 15\ M^{-1}\ sec^{-1}$) is an even poorer nucleophile because the protonation of one nitrogen reduces the basicity of the adjacent nitrogen (the pK_a value for $H_2(EDTA)^{2-}$ is 4.1 units less than that for $H(EDTA)^{3-}$). The kinetic studies of the autocatalysis reactions show that $EDTA^{4-}$ can react more readily with $CuH_{-2}L_2^{2-}$ than it does with $CuH_{-2}L^-$. The peculiar pH maximum in Figure 2 might be explained by a somewhat different mechanism than given in eq 3 and 4 if $H(EDTA)^{3-}$ is assumed to be the major reactant with $CuH_{-2}L_2^{2-}$ rather than $EDTA^{4-}$. In this mechanism eq 3 and 4 would be replaced by eq 10 and 11, and the steps in eq 2 and 5 would be the same.

$$CuH_{-2}L_2^{2-} \rightleftharpoons [CuH_{-2}L_2^{2-}]^* \quad (10)$$

$$[CuH_{-2}L_2^{2-}]^* + H(EDTA)^{3-} \rightleftharpoons Cu(H_{-1}L)EDTA^{4-} + L^- \quad (11)$$

As in the previous case a limiting step is needed at high EDTA concentrations and this is provided in eq 10 where $[CuH_{-2}L_2^{2-}]^*$ is a reactive form with only one amine nitrogen and two peptide nitrogens coordinated to Cu(II). In eq 11 $H(EDTA)^{3-}$ acts both as a nucleophile and as an acid. Such a double role has been suggested for the unusual effectiveness of $H_2PO_4^-$ in its reaction with $NiH_{-2}L^-$ (*i.e.*, $H_2PO_4^-$ as a coordinating acid).[9] The kinetic data can be resolved using reactions 2, 10, 11, and 5 in much the same manner as with reactions 2–5. However, there are two reasons which indicate that the path in eq 10 and 11 is unlikely. First, $H(EDTA)^{3-}$ is not an effective coordinating acid with $CuH_{-2}L^-$ and would not be expected to be with $CuH_{-2}L_2^{2-}$ unless there were a juxtaposition of the $H(EDTA)^{3-}$ proton and a $[CuH_{-2}L_2^{2-}]^*$ peptide nitrogen in that reaction. In short, a molecular rearrangement specific for $CuH_{-2}L_2^{2-}$ must be proposed for this path. Second, if $H(EDTA)^{3-}$ were acting as a coordinating acid with $CuH_{-2}L_2^{2-}$, then the same behavior would be expected for other ligands. This was tested with diethylenetriaminepentaacetate (DTPA) as the exchanging ligand. The DTPA points in Figure 2 show the same behavior below pH 9.7 as the EDTA reactions. Above pH 9.7, however, the rate constants for DTPA (run under identical conditions) are about a factor of 2 larger than for EDTA. The pK_a value of $H(DTPA)^{4-}$ is 10.42 compared to a value of 10.26 for $H(EDTA)^{3-}$ and if the ligands were acting as coordinating acids, the rate constants in the DTPA experiments would be smaller, not larger, than for EDTA. Also, there is unlikely to be a second specific molecular rearrangement which would put the proton of $H(DTPA)^{3-}$ in juxtaposition with a peptide nitrogen of $[CuH_{-2}L_2^{2-}]^*$. On the other hand the mechanism in eq 3 and 4 would account for the enhanced reactivity of DTPA. The $H(DTPA)^{4-}$ species would be expected to be a better nucleophile than $H(EDTA)^{3-}$ because the proton can be more distant from the aminocarboxylate group which is reacting. Thus, one proton does not decrease the basicity of the ligand nearly as much as is the case with EDTA (the pK_a value for $H_2(DTPA)^{3-}$ is 1.7 units less than for $H(DTPA)^{4-}$ compared to a 4.1-unit difference for the corresponding EDTA species). The DTPA experiments were run only to test the proposed mechanism and the individual rate constants were not resolved.

An additional point can be made in regard to the proposed mechanism in eq 3 and 4. It was not possible to fit the data if these two reactions were combined into one step. Therefore, it appears that the reaction in eq 3 must precede the $EDTA^{4-}$ attack. The EDTA does not initiate the cleavage of a peptide nitrogen bond to copper but rather takes advantage of such a reaction.

The fact that EDTA is much more reactive with the bis-triglycine complex of copper seems at first inconsistent with the steric effects found for the mono-triglycine complex.[1] However, the bis complex is more easily converted to a form which does not sterically hinder the most effective path for nucleophilic attack, which is *via* nitrogen coordination by EDTA to a planar copper site. The multiple coordination in the mono-triglycine complex forces all its coordinate groups to bond in one plane as is shown in structure I of Figure 5.

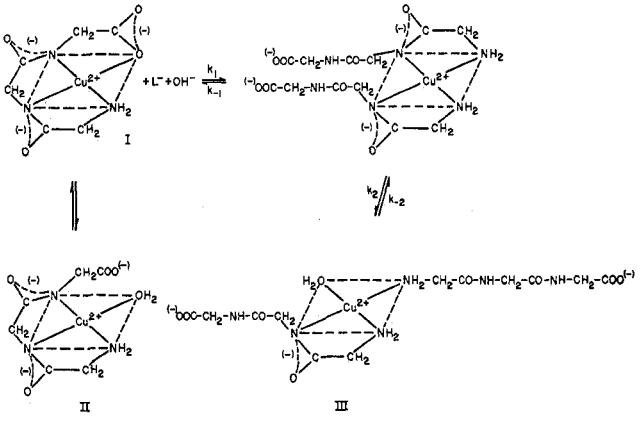

Figure 5.—Proposed structures for the first two steps in the mechanism of triglycine autocatalysis.

Upon removal of the carboxylate group from the coordination plane (structure II), the planar site occupied by water is readily attacked by primary and secondary amines but tertiary amines are sterically hindered due to limitations imposed by the methylene group on the adjacent peptide nitrogen and the hydrogens on the adjacent amine terminal. Therefore, the carboxylate group and one peptide nitrogen need to be removed from the coordination plane of copper in order to allow EDTA to react in this manner. On the other hand, the bis-triglycine complex needs to free only a peptide nitrogen to permit a similar nucleophilic reaction with EDTA since, as is seen in structure III, the monodentate triglycine moiety is free to move thus accommodating

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tertiary nitrogen attack at the planar site occupied by water. Thus, both $CuH_{-1}L$ and $CuH_{-1}L_2^-$ are very reactive with EDTA. Comparison of the log K_H values, 6.7 (for $CuH_{-2}L^- + H^+ \rightleftarrows CuH_{-1}L$) and 8.7 (for $CuH_{-2}L_2^{2-} + H^+ \rightleftarrows CuH_{-1}L_2^-$), gives a thermodynamic indication of the relative ease of formation of the reactive species. Therefore, the postulated role of triglycine in the autocatalysis reaction is to facilitate the formation of a complex with only one Cu–N(peptide) bond.

Triglycine autocatalysis has also been observed[8] in the reaction of nickel–triglycine ($NiH_{-2}L^-$) with EDTA but the mechanism was not established.

Considerable experimental evidence indicates that the bonding of Cu(II) to serum albumin involves the α-amino terminal plus one or more peptide nitrogen atoms,[10,11] in a manner similar to the bonding in copper–triglycine. Mixed complexes of copper(II) with serum albumin and several amino acids have been shown to exist in the blood in equilibrium with the copper(II)–serum albumin complex[12–16] (the major fraction of labile copper(II) in the blood). These mixed complexes have been postulated to be important intermediates in the transfer of copper from the blood to various organs and tissues.[17–20] In the present work the transfer of copper(II) from a mixed copper(II)–tripeptide complex is much faster than from the parent mono complex and this type of kinetic behavior may bear some relevance to the function of the mixed copper(II)–serum albumin–amino acid complexes in the biological transport of copper.

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Temperature-Dependent Tetragonal Distortion in Some Thermochromic *N,N*-Diethylethylenediamine Complexes of Copper(II)

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The temperature-dependent infrared, far-infrared, and electronic spectra and magnetism of a series of thermochromic copper complexes of *N,N*-diethylethylenediamine (*asym*-$(C_2H_5)_2$en) are reported. These data, together with some existing esr data, confirm that the thermochromic behavior of these complexes arises through a temperature-dependent axial interaction between the anion and the CuN_4 plane, with the more square form being favored at lower temperature. In the series $Cu(asym\text{-}(C_2H_5)_2en)_2X_2$ where $X^- = ClO_4^-$, BF_4^-, and NO_3^-, the thermochromism of the tetrafluoroborate and nitrate complexes is demonstrated for the first time. In the case of the nitrate, two mutually interconvertible isomers, one square and one six-coordinate, have been isolated and identified.

The study of thermochromic materials (compounds whose color is temperature dependent) has excited interest for some time.[1] A number of such complexes were reported in a study of the products of reaction of some copper salts with various *N*-alkyl-substituted ethylenediamines.[2] Of particular interest has been the study of complexes[3–5] of *N,N*-diethylethylenediamine (*asym*-$(C_2H_5)_2$en) of molecular formula $Cu(asym\text{-}(C_2H_5)_2en)_2X_2$. The perchlorate derivative ($X^- = ClO_4^-$) is red at room temperature but turns blue above about 40°.[2,4,5] The color change is reversible. Thermochromic behavior was sought for other copper complexes of this ligand but none was found.[4] In our hands both the tetrafluoroborate salt ($X^- = BF_4^-$) and the nitrate ($X^- = NO_3^-$) were found to be reversibly thermochromic. In the latter case, two isomers, a red and a purple form, have been separately established. The electronic, vibrational, and magnetic properties of these complexes are reported here and interpreted in terms of varying tetragonal distortion.

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Experimental Section

All the complexes have been reported before.[2,6] The tetrafluoroborate complex is sufficiently thermochromic to change color (from red to purple) on contact with any warm surface, such as living skin. Since it is difficult to believe that earlier workers[4,5] could have missed this thermochromism, we assume that our preparation, which probably differs from earlier preparations (these were not adequately described so cannot be reproduced), gives rise to the product in a different crystalline phase than had previously been observed. The preparation is given below. Electronic spectra were recorded as transmittance

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