Kinetics and mechanism of the reactions of Cu(II)-N,N-Diglycylethylenediamine with triethylenetetramine and Ethylenediaminetetraacetate
by Presley Kirkland Mitchell

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Chemistry
Montana State University

Abstract:
The substitution kinetics and mechanisms of copper(II)-N,N'-diglycylethylenediamine (CuH-2DGEN) with triethylenetetramine (TRIEN) and ethylenediaminetetraacetate (EDTA) ion were investigated. The overall rate expression for each reactant was resolved, and the rate constants for the reaction pathways were determined.

The reaction between Copper(II)-N,N'-diglycylethylenediamine and triethylenetetramine proceeded via a nucleophilic and general acid catalysis pathway. The rate constants are kT = 650 M^-1 s^-1, kHT = 210 M^-1 s^-1, kH2T = 87 M^-1 s^-1 and kH3T = 2100 M^-1 s^-1.

The reaction between copper(II)-N,N'-diglycylethyethylenediamine and ethylenediaminetetraacetate ion proceed via a general acid catalysis pathway. The rate constants for the mono- and diprotonated species are kHEDTA = 56 M^-1 s^_1 and kH2EDTA = 1.1 x 10^5 M^-1 s^-1.

Other replacing ligand independent rate constants that are applicable to both systems are kd = 0.043 s^-1 , kH3BO3 = 116 M^-1 s^_1 and kH3O = 1*5 x 10' M-' s .

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APPROVAL

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Presley Kirkland Mitchell

This thesis has been read by each member of the thesis committee and has been found to be satisfactory regarding content, English usage, format, citations, bibliographic style, and consistency, and is ready for submission to the College of Graduate Studies.

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Date Feb. 24, 1983

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ABSTRACT

The substitution kinetics and mechanisms of copper(II)-N,N'-diglycylethylenediamine ($CuH_{-2}DGEN$) with triethylenetetramine (TRIEN) and ethylenediaminetetraacetate (EDTA) ion were investigated. The overall rate expression for each reactant was resolved, and the rate constants for the reaction pathways were determined.

The reaction between copper(II)-N,N'-diglycylethylenediamine and triethylenetetramine proceeded *via* a nucleophilic and general acid catalysis pathway. The rate constants are k_T = 650 M^{-1} s^{-1}, k_{HT} = 210 M^{-1} s^{-1}, k_{H_2T} = 87 M^{-1} s^{-1} and k_{H_3T} = 2100 M^{-1} s^{-1}.

The reaction between copper(II)-N,N'-diglycylethyethylenediamine and ethylenediaminetetraacetate ion proceed *via* a general acid catalysis pathway. The rate constants for the mono- and diprotonated species are k_{HEDTA} = 56 M^{-1} s^{-1} and k_{H_2EDTA} = 1.1 x 10^5 M^{-1} s^{-1}.

Other replacing ligand independent rate constants that are applicable to both systems are k_d = 0.043 s^{-1}, $k_{H_3BO_3}$ = 116 M^{-1} s^{-1} and k_{H_3O} = 1.5 x 10^7 M^{-1} s^{-1}.

CHAPTER 1

INTRODUCTION

The kinetics and mechanisms of the transfer of copper(II) between peptide and amino acid complexes are important to the understanding of the biological transport of this metal ion.

The imbalance of copper within the biological system has been associated with an assortment of diseases. For example, the rare inherited Wilson's disease involves the inability to excrete copper and is characterized by high free copper levels (1). The treatment of this disease involves the removal of copper *via* copper chelating agents such as ethylenediaminetetraacetate ion and D-penicillamine (1). Triethylenetetramine (TRIEN) was also found to be an effective chelating agent (2).

Metal peptide or oligopeptide complexes have the general formula $M(H_{-n}L)$, where there are n peptide or amide groups bonded to the metal ion. Evidence for metal-N(peptide) bonding in diglycine, triglycine and tetraglycine have been verified by infrared and visible spectroscopy, as well as potentiometric measurements (3). The results of X-ray crystallographic studies (1) have shown, unequivocally, the peptide proton displacement in the solid and the coordination of the resulting negative peptide groups to metal ions.

The chemical kinetic behavior of the metal-N(peptide) bonds have some interesting properties. Although the N(peptide) group is a strong donor that is tightly bound to metal ions, it tends to be the group displaced in protonation, dissociation and nucleophilic

reactions. The configurations of copper-triglycine, copper-glyclglycyl-L-histidine and copper-tetraglycine are shown in Figure 1. These examples will aid in understanding kinetic variations that occur in metal-N(peptide) complexes. The above complexes are unique because they contain different terminally bonded groups. These structural differences result in different reaction kinetics.

The various reaction pathways that occur with metal-N(peptide) complexes include the solvent dissociation, nucleophilic and protonation pathways (4).

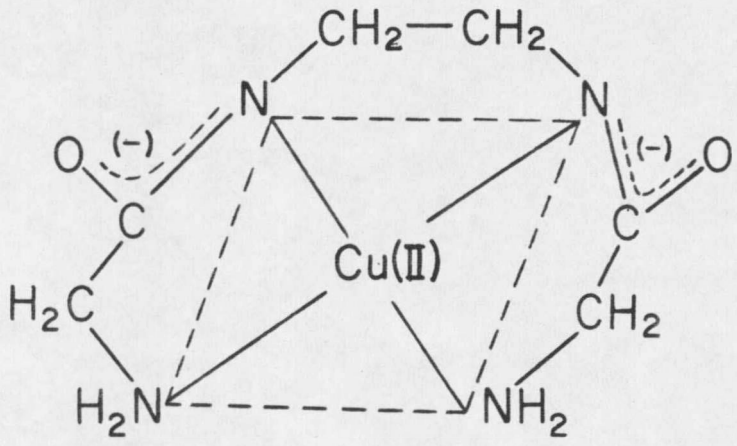
The solvent dissociative pathway is independent of the replacing ligand concentration. The solvent, water in this discussion and study, can act as an acid or nucleophile, leading to the cleavage of the metal-N(peptide) bond. Once this bond breaks, other water molecules will rapidly transfer a proton to the very basic free deprotonated-peptide nitrogen. Equations 1 and 2 illustrate the reactions in which solvent dissociation is believed to occur (5),

$$M(H_{-n}L) + H_2O \underset{k_{-d}}{\overset{k_d}{\rightleftharpoons}} M(H_{-n}L^{*})(H_2O) \qquad (1)$$

$$M(H_{-n}L^{*})(H_2O) + H_2O \xrightarrow{\text{rapid}} M(H_{-n+1}L)(H_2O) + OH^{-} \qquad (2)$$

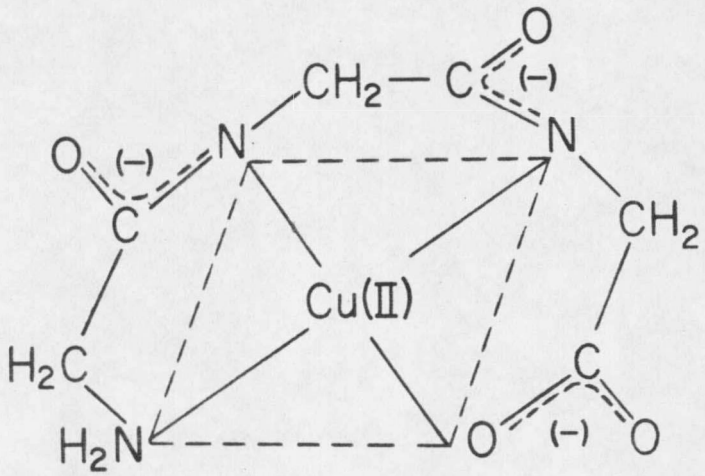
where $(H_{-n}L^{*})$ refers to the presence of a free deprotonated-peptide nitrogen.

The dissociative rate constant for copper triglycine was experimentally found to be 0.12 s^{-1} (6). This k_d term is associated



$CuH_{-2}DGEN$

Copper(II)-N,N'-Diglycylethylenediamine



$Cu(H_2GGG)^-$

Copper(II)-Triglycine

Figure 1. Structures of several copper(II) complexes.