

Multidentate Ligand Kinetics. VII. The Stepwise Nature of the Unwrapping and Transfer of Ethylenediaminetetraacetate from Nickel(II) to Copper(II)

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The reaction between copper(II) and nickel(II)-EDTA is studied at 25° over a 10^5 M range of copper concentrations between pH 2 and pH 7 and at ionic strengths of 0.1, 0.4, 0.8, and 1.25 M. The reaction is first order in the concentration of the nickel complex, but the reaction order with respect to copper decreases as the copper concentration increases. At pH 4.5 there are several fluctuations between first-order and zero-order copper dependence. The reaction rate is sensitive to $[H^+]$ when the copper dependence is zero order. When the copper dependence is first order, the reaction rate constant is not pH sensitive below pH 5.5, but the rate constant increases above pH 5.5. A stepwise mechanism with the unwrapping of an iminodiacetate group from nickel-EDTA followed by reaction with copper and proceeding through a nickel iminodiacetate-copper iminodiacetate reaction intermediate explains the data. In the proposed mechanism the rate-determining step shifts to the half-unwrapping of EDTA from nickel as the concentration of copper is varied from 10^{-5} to 10^{-2} M. This changes the reaction order without a change in the nature of the reactants. Above 10^{-2} M copper the reactants begin to change owing to a weak complex between nickel-EDTA and copper, and another change of reaction order is superimposed on the initial one. Mechanisms based on the stepwise unwrapping of EDTA from one metal and the stepwise transfer to the second metal can be analyzed in terms of the stability of the bonded segments, the rate of substitution of the aquo metal ion, and the electrostatic and steric repulsions of the groups involved. Changes of reaction order should be expected for multidentate ligand exchange reactions, and unless the complete stepwise mechanism is considered care must be exercised in the extrapolation of rate data from one concentration level to another.

Introduction

Earlier work¹ showed that the exchange reaction between copper ion and nickel-EDTA was first order



in the concentration of each reactant. Many EDTA-exchange reactions have a similar kinetic dependence so that eq. 2 is a general rate expression.²⁻⁴

(1) T. J. Bydalek and D. W. Margerum, *J. Am. Chem. Soc.*, **83**, 4326 (1961).

(2) D. W. Margerum and T. J. Bydalek, *Inorg. Chem.*, **1**, 852 (1962).

(3) D. W. Margerum, *Record Chem. Progr.* (Kresge-Hooker Sci. Lib.), **24**, 237 (1963).

(4) See a series of papers by N. Tanaka including the following recent contributions: (a) N. Tanaka, H. Osawa, and M. Kamada, *Bull. Chem. Soc. Japan*, **36**, 530 (1963); (b) N. Tanaka and H. Ogino, *ibid.*, **36**, 175 (1963); (c) N. Tanaka, H. Osawa, and M. Kamada, *ibid.*, **36**, 67 (1963).

$$\text{exchange rate} = k_M^{M^X} [M'] [MY] \quad (2)$$

Previously, emphasis has been placed on the evidence for a dinuclear reaction intermediate of Ni-EDTA-Cu where one nitrogen atom is bonded to nickel and the other to copper. The values of the second-order rate constants for the reaction of metal ions with nickel-EDTA have been correlated to the stability constant of each ion with an iminodiacetate segment of EDTA.³ Other evidence supports this mechanism.^{5,6} Thus, there is a considerable body of data in accord with a reaction mechanism having an iminodiacetate segment of EDTA unwrapped from nickel and bonded to the reacting metal ion. Until now most of the kinetic evidence has been focused on the situation in which the rate-determining step occurs after the formation of this type of dinuclear intermediate.

In the present study of the reaction in eq. 1, the copper concentration was varied from 10^{-5} to 0.3 M under a variety of conditions of pH and ionic strength. As the copper concentration was increased, its kinetic dependence changed from first order to zero order. In some cases as copper was increased above 10^{-2} M a first-order copper dependence started to reappear but disappeared once more.

The fluctuations of the reaction order with copper concentration do not contradict but rather confirm and permit an expanded analysis of the earlier interpretations of the stepwise nature of EDTA-exchange reactions. The kinetic behavior as the concentration of copper is increased suggests that the rate-determining step can be shifted to earlier positions in the reaction path, namely, the half-unwrapping of EDTA from nickel or from a weak copper-nickel EDTA complex.

The first change of reaction order takes place without any change in the nature of the observable reactants and appears to be due only to a shift of the relative concentrations of unstable reaction intermediates. This type of kinetic behavior occurs in the acid dissociation of $\text{Ni}(\text{en})^{+2}$ ⁷ and well-known examples occur in organic systems.⁸

The last change in reaction order is not an uncommon kinetic phenomenon. It is frequently observed when a rapid combination of two reactants gives a new reactant species. In fact, even a transition from first to zero order, again to first order and back to zero order, has been found in enzymatic catalysis where saturation of two enzyme sites occurs in succession.⁹

(5) T. J. Bydalek and D. W. Margerum, *Inorg. Chem.*, **2**, 678 (1963).

(6) D. W. Margerum and T. J. Bydalek, *ibid.*, **2**, 683 (1963).

(7) A. K. S. Ahmed and R. G. Wilkins, *J. Chem. Soc.*, 3700 (1959).

(8) E. D. Hughes, C. K. Ingold, and R. J. Reed, *ibid.*, 2400 (1950).

(9) C. G. Trowbridge, A. Krehbiel, and M. Laskowski, Jr., *Biochemistry*, **2**, 843 (1963).

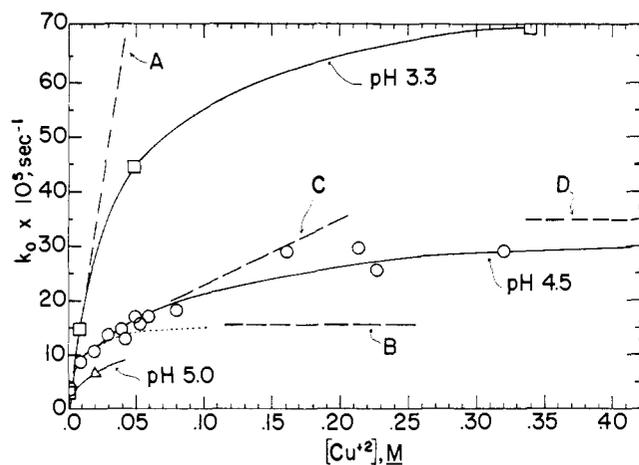


Figure 1. Effect of hydrogen ion concentration and varying excess copper concentration on the observed first-order rate constant (25.0°, $\mu = 1.25$). Table I indicates pH variation.

Experimental Section

Reaction rates were followed using a Beckman DU spectrophotometer with cell compartments thermostated at $25.0 \pm 0.1^\circ$. Ionic strength was controlled by NaClO_4 and pH was controlled by a borate-mannitol buffer (10^{-2} to $10^{-3} M$ borate) or a 2,6-lutidinium perchlorate buffer (10^{-2} to $10^{-3} M$).

In a few cases a stopped flow apparatus fitted to the DU optical system permitted reactants to be mixed within a few milliseconds and the rate was followed with an oscilloscope. Most reactions were slow and the stopped flow apparatus was used only to check the rate of formation of the mixed complex.

All reactions studied had a first-order dependence in nickel-EDTA while the dependence in copper varied from zero to first order. Kinetic data were based on the appearance of copper-EDTA using ultraviolet or visible spectrophotometry. For reactions with a large excess of copper ion the observed rate constant, k_o ,

$$\text{rate} = k_o [\text{NiY}_T] \quad (3)$$

may or may not vary with the excess concentration. (In eq. 3 the term NiY_T refers to the total of all forms of nickel-EDTA, $[\text{NiY}_T] = [\text{NiY}^{2-}] + [\text{NiHY}^-] + [\text{NiH}_2\text{Y}] + [\text{NiYCu}]$.) Some reactions were studied at low concentrations without excess copper ion giving a second-order rate constant k . Suitable equations for

$$\text{rate} = k[\text{NiY}_T][\text{Cu}_T] - k'[\text{CuY}_T][\text{NiT}] \quad (4)$$

reversible second-order reactions were used¹⁰ and the calculations were done on an IBM 7090 computer.

A number of facts were checked to be certain that the change of absorbance during the reaction corresponded to eq. 1 in both the ultraviolet and visible regions and that changes in the reaction order of copper were not caused by extraneous factors.

(1) Reactions observed at 260, 270, 300, and 735 $m\mu$ had identical rate constants for the same copper concentration.

(2) A check for possible trace metal contamination, tests of the sequence of addition of reactants, the use of KNO_3 instead of NaClO_4 for ionic strength control,

(10) A. F. Frost and R. G. Pearson, "Kinetics and Mechanisms," John Wiley and Sons, Inc., New York, N. Y., 1953, pp. 174, 175.

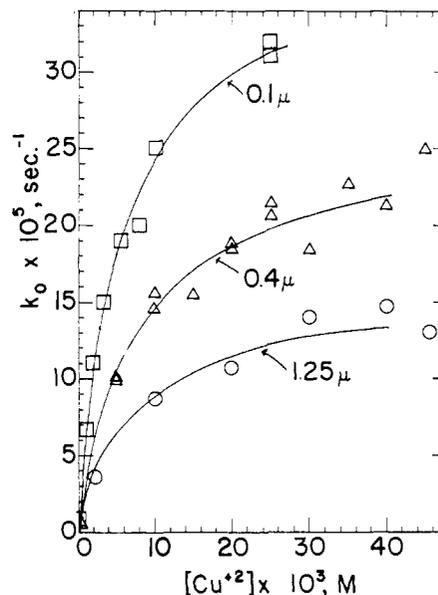


Figure 2. The effect of ionic strength and varying excess copper concentration on the observed first-order rate constant (25.0°, pH 4.5); curves constructed from values in Table III.

and the use of two different buffers all showed that none of these factors interfered.

(3) Dimers of unhydrolyzed Cu(II) are known in some solvents but do not exist in water.¹¹ Little if any copper perchlorate bonding is reported even in the solid state.¹²

(4) Repetitive spectrophotometric scans of reaction mixtures gave no evidence of any buildup and decay of reaction intermediates. Thus, isosbestic points were observed at 225 $m\mu$ ($4 \times 10^{-4} M \text{ Cu(II)}$) and at 370 $m\mu$ ($4 \times 10^{-3} M \text{ Cu(II)}$).

Individual reactions gave simple kinetic plots at all wave lengths. This was true even at 0.3 $M \text{ Cu(II)}$. The only unusual behavior was a very rapid absorbance jump that occurred upon mixing the reactants when $\text{Cu(II)} > 10^{-2} M$. This does correspond to an alteration of eq. 1 and is discussed in the next section.

Results and Discussion

Variation of Reaction Order with Copper and pH. Figure 1 shows the effect of copper concentration on the observed first-order rate constant (eq. 3) at an ionic strength of 1.25 M . Table I shows the pH variations for these data. The straight line marked A on the left-hand side of the figure represents eq. 5 as reported

$$k_o = k_{\text{Cu}}^{\text{NiY}} [\text{Cu}^{2+}] \quad (5)$$

previously.¹ This equation was valid up to 0.02 M copper at pH 2.9 and held even at pH 4 for 0.004 M copper. However, an inspection of the three curves at pH 3.3, 4.5, and 5.0 shows that the higher the pH, the lower is the concentration of copper needed to cause deviation from the first-order relationship in eq. 5.

Data in Figure 2 at pH 4.5 show how the dependence of k_o upon copper approaches a plateau around 0.02 M copper representing a zero-order copper dependence. This shift in order occurred without significant change in the nature of the reactants. This is a vital fact be-

(11) R. L. Martin and A. Whaley, *J. Chem. Soc.*, 1394 (1958).

(12) B. J. Hathaway and A. E. Underhill, *ibid.*, 3091 (1961).

Table I. The Effect of pH, Ionic Strength, and Varying Excess of Copper Ion Concentration on the Observed First-Order Rate Constant at 25.0°

μ	$[\text{Cu}^{+2}], M$	$[\text{NiY}^{-2}], M$	pH	$k_o, \text{sec.}^{-1}$
1.25	9.75×10^{-3}	1.24×10^{-4}	3.27	1.5×10^{-4}
	4.88×10^{-2}		3.32	4.4×10^{-4}
	3.40×10^{-1}	1.19×10^{-2}	3.30	7.0×10^{-4}
	1.95×10^{-3}	1.24×10^{-4}	3.09	3.2×10^{-5}
	2.14×10^{-2}	3.31×10^{-3}	4.96	6.8×10^{-5}
	2.20×10^{-3}	1.14×10^{-3}	4.50	3.6×10^{-5}
	1.00×10^{-2}	8.28×10^{-3}	4.50	8.7×10^{-5}
	2.00×10^{-2}	8.28×10^{-4}	4.58	11×10^{-5}
	2.99×10^{-2}		4.53	14×10^{-5}
	3.99×10^{-2}	3.31×10^{-3}	4.64	15×10^{-5}
	4.28×10^{-2}		4.63	13×10^{-5}
	4.99×10^{-2}	8.28×10^{-3}	4.62	17×10^{-5}
	5.35×10^{-2}	3.31×10^{-3}	4.64	16×10^{-5}
	5.98×10^{-2}		4.54	17×10^{-5}
	7.98×10^{-2}		4.57	18×10^{-5}
	16.1×10^{-2}	4.14×10^{-3}	4.31	29×10^{-5}
	21.4×10^{-2}		4.21	30×10^{-5}
22.7×10^{-2}	5.95×10^{-3}	4.40	26×10^{-5}	
32.1×10^{-2}	4.14×10^{-3}	3.93	29×10^{-5}	
0.8	1.20×10^{-3}	1.24×10^{-4}	4.82	2.6×10^{-5}
	9.75×10^{-3}		4.76	8.7×10^{-5}
	4.88×10^{-2}		4.73	1.4×10^{-4}
0.4	1.2×10^{-4}	1.2×10^{-4}	4.52	4.7×10^{-6}
	1.2×10^{-3}		4.84	3.4×10^{-5}
	4.99×10^{-3}	4.14×10^{-4}	4.43	1.1×10^{-4}
			4.42	1.0×10^{-4}
	1.00×10^{-2}		4.47	1.6×10^{-4}
			4.46	1.5×10^{-4}
	1.50×10^{-2}	8.28×10^{-4}	4.44	1.6×10^{-4}
	2.00×10^{-2}	1.03×10^{-3}	4.44	1.8×10^{-4}
		8.28×10^{-4}	4.43	1.9×10^{-4}
	2.50×10^{-2}	1.03×10^{-3}	4.51	2.2×10^{-4}
0.1			4.54	2.1×10^{-4}
	3.00×10^{-2}	8.28×10^{-4}	4.52	1.8×10^{-4}
	3.50×10^{-2}		4.45	2.3×10^{-4}
	4.00×10^{-2}		4.53	2.1×10^{-4}
	4.50×10^{-2}		4.52	2.5×10^{-4}
	1.2×10^{-4}	1.24×10^{-4}	4.64	9.4×10^{-6}
	1.2×10^{-3}		4.67	6.7×10^{-5}
	2.27×10^{-3}	4.14×10^{-4}	4.50	1.1×10^{-4}
	3.40×10^{-3}		4.50	1.5×10^{-4}
	5.68×10^{-3}		4.51	1.9×10^{-4}
7.95×10^{-3}		4.56	2.0×10^{-4}	
1.02×10^{-2}		4.51	2.5×10^{-4}	
2.50×10^{-2}	8.28×10^{-4}	4.55	3.1×10^{-4}	
2.50×10^{-2}		4.48	3.2×10^{-4}	

cause the NiYCu species observed at higher copper concentrations cannot explain the initial change in reaction order.

The data in Figure 2 can be explained in terms of eq. 6 where $a \gg b[\text{Cu}^{+2}]$ at $10^{-5} M$ copper but $b[\text{Cu}^{+2}]$

$$k_o = \frac{ab[\text{Cu}^{+2}]}{a + b[\text{Cu}^{+2}]} \quad (6)$$

$> a$ at $0.02 M$ copper. Using eq. 6 and the definition that $k[\text{Cu}^{+2}] = k_o$ permits eq. 7 to be written in a form suitable for graphical plotting in Figure 3.

$$\frac{1}{k} = \frac{1}{b} + \frac{[\text{Cu}^{+2}]}{a} \quad (7)$$

For each ionic strength in Figure 3 the linear relationship fits eq. 6 and 7 and is in agreement with the transition from a first-order to zero-order copper dependence between 10^{-4} and $4 \times 10^{-2} M$ copper. These data are all at $\text{pH } 4.5 \pm 0.1$, and the scatter observed is due to

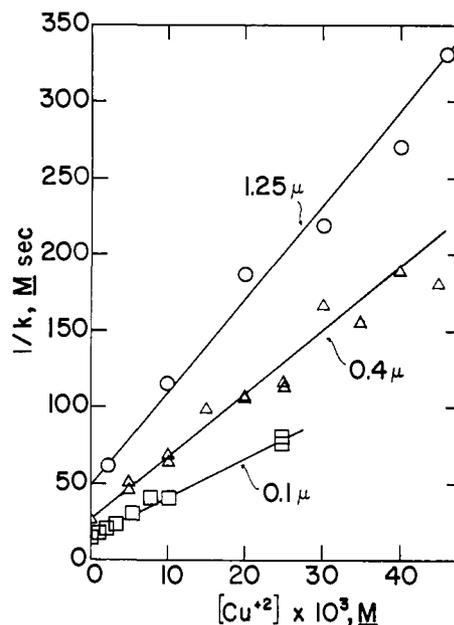


Figure 3. Resolution of k_{CuNiY} and k_{12} from second-order rate constants (25.0°, pH 4.5). Second-order constants are calculated from data in Table I. Deviations at high copper are expected, as seen in Figure 4 and discussed in text.

the high pH dependence of the zero-order rate constant.

Figure 1 shows that the plateau B expected from the graphical evaluation in Figure 3 never quite materialized. Instead, another first-order dependence in copper seemed to appear as represented by line C. As the copper ion concentration was increased above $0.1\text{--}0.2 M$, this dependence was superseded by a new plateau. As will be shown, the maximum value of k_o appears to approach the horizontal line represented by D.

The deviation of the points along lines C and D from the initial change in order from A to B is much greater than the experimental error. This is difficult to see in Figure 2 but is readily seen in Figure 4, which extends the plot in Figure 3 to almost a 10-fold increase in copper ion concentration. The data cannot be explained in terms of a single transition from a first-order to a zero-order copper dependence.

An Observable NiYCu Species. When the reactions were initiated with greater than $10^{-2} M$ copper, an immediate jump in absorbance at $735 m\mu$ occurred. After the reaction was complete, however, the absorbance corresponded to that expected for copper-EDTA. Assuming that the absorbance jump, A_j (eq. 8), is caused by a 1:1 complex of NiY⁻² and Cu⁺²,

$$A_j = A_{\text{mixture}} - \sum A_{\text{reactants}} = (\epsilon_{\text{NiYCu}} - \epsilon_{\text{Cu}} - \epsilon_{\text{NiY}})b[\text{NiYCu}] \quad (8)$$

it can be shown that eq. 9 holds, where b is the cell

$$\frac{[\text{NiY}_T]b}{A_j} = \frac{1}{(\epsilon_{\text{NiYCu}} - \epsilon_{\text{Cu}} - \epsilon_{\text{NiY}})K_{\text{NiYCu}}[\text{Cu}^{+2}]} + \frac{1}{(\epsilon_{\text{NiYCu}} - \epsilon_{\text{Cu}} - \epsilon_{\text{NiY}})} \quad (9)$$

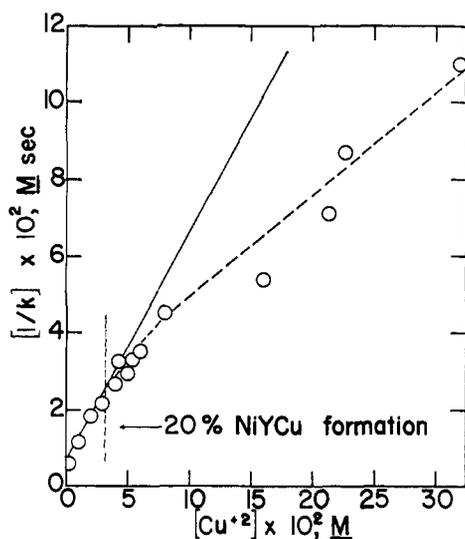


Figure 4. Deviation from k_{12} at very high copper concentration (25.0°, pH 4.5, $\mu = 1.25$). Second-order constants are calculated from data in Table I.

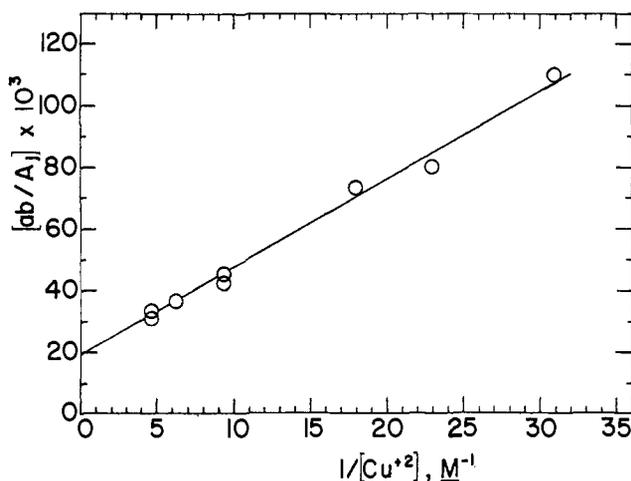


Figure 5. Resolution of absorbance jump data to show stoichiometry, molar absorptivity, and stability constant of species (25.0°, $\mu = 1.25$, λ 735 m μ , $a = [\text{NiY}^-]$, $b = \text{cell path}$).

path, ϵ_{NiYCu} is the molar absorptivity of the NiYCu complex, and K_{NiYCu} is defined by eq. 10. Figure 5

$$K_{\text{NiYCu}} = \frac{[\text{NiYCu}]}{[\text{NiY}^-][\text{Cu}^{+2}]} = 6.8 \quad (25^\circ, 1.25 \mu) \quad (10)$$

gives the plot of eq. 9. The linear dependence supports the assumption of a 1:1 complex. The intercept gives a value of 64 for ϵ_{NiYCu} (735 m μ) and the slope yields a value of 6.8 for K_{NiYCu} .

The NiYCu complex formed much too rapidly to be a species with copper bonded to a nitrogen atom of EDTA. Mixing the reactants by means of a stopped flow apparatus showed that the absorbance jump occurred within the instrumental time limitation of a few milliseconds. A comparison can be made to the sluggish reaction of copper with the nitrilotriacetato-nickelate(II) complex.¹³ The same number and type of donor bonds to nickel must be broken in the half-unwrapping of EDTA as in the dissociation steps of the

(13) T. J. Bydalek and M. L. Blomster, *Inorg. Chem.*, **3**, 667 (1964).

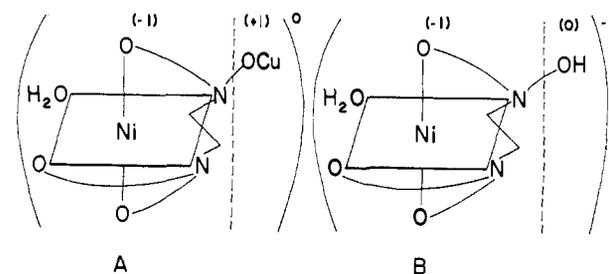


Figure 6. Proposed structure of an observable nickel-EDTA-copper complex (A) which forms when copper is greater than 10^{-2} M and forms rapidly. The structure is compared to that of the nickel-EDTA-hydrogen ion complex (B).

nitrilotriacetate complex. The latter has a half-life of 700 min. at pH 4.5, or for the copper-assisted path at 0.1 M copper, a half-life of 74 min. Therefore, the fact that the formation of the NiYCu species requires less than a few milliseconds means that a nickel-nitrogen bond cleavage is not involved. This contention is further supported by the general sluggishness of the first nitrogen cleavage from metal EDTA complexes shown by n.m.r. studies.¹⁴

Because the significant absorbance jump occurred in the visible region, the NiYCu species cannot be readily dismissed as an ion pair between $\text{NiY}^{-2}(\text{aq})$ and $\text{Cu}^{+2}(\text{aq})$. The value of $\epsilon_{\text{NiYCu}} = 64$ (735 m μ) is in approximate agreement with the molar absorptivity of copper acetate (ϵ 25 at 735 m μ) and of nickel-EDTA (ϵ 2.5 at 735 m μ). Therefore a NiYCu species is proposed where copper is bonded in a manner similar to that proposed for hydrogen ion in NiYH^- .^{15,16} Figure 6 compares the proposed structure of NiYCu and NiYH⁻. These complexes can form very rapidly because NiY^{-2} may have a free acetate group or, if not, will react rapidly to free a single acetate group from nickel coordination. Also, the rate of coordination to copper is fast.

If the structure in Figure 6A is correct, then the ratio of the stability constants of NiYCu (see eq. 10) and of NiYH ($K_{\text{NiYH}} = [\text{NiYH}^-]/[\text{NiY}^{-2}][\text{H}^+]$) should correspond to the relative stabilities of Cu^{+2} and of H^+ bonded to an acetate group. As indicated in Figure 6A, there also is a net electrostatic attraction of the copper acetate branch for the rest of the ion which is not present for NiYH in Figure 6B. This K_{el} term is estimated to be equal to at least 3 (using a distance of about 6 Å. between charge centers and the dielectric constant of water). Equations 11 and 12 indicate

$$\text{exptl. } \frac{K_{\text{NiYCu}}}{K_{\text{NiYH}}} = \frac{6.8}{0.82 \times 10^3} = 8.3 \times 10^{-3} \quad (11)$$

$$\text{calcd. } \frac{K_{\text{NiYCu}}}{K_{\text{NiYH}}} = K_{\text{el}} \frac{K_{\text{CuAc}}}{K_{\text{HAc}}} = 3 \times \frac{10^{1.67}}{10^{4.61}} = 3.4 \times 10^{-3} \quad (12)$$

that within the accuracy of this type of calculation the stability of the NiYCu intermediate does correspond to the expected value.

Thus, there is evidence for an observable reaction intermediate, NiYCu, and the structure proposed in

(14) R. J. Day and C. N. Reilley, *Anal. Chem.*, **36**, 1073 (1964).

(15) G. Schwarzenbach and J. Heller, *Helv. Chim. Acta*, **34**, 567 (1951).

(16) G. S. Smith and J. L. Hoard, *J. Am. Chem. Soc.*, **81**, 556 (1959).

Figure 6A is in good agreement with (1) the kinetic requirements, (2) the order of magnitude of ϵ_{NiYCu} and (3) the estimated stability of such a species.

It must be emphasized that the NiYCu species in Figure 6A appears only at high copper concentrations and that it is not the same as the previously proposed dinuclear reaction intermediate which is so important in controlling the rate of transfer of EDTA from one metal to another at low concentrations. The species in Figure 6A is a precursor to the latter reaction intermediate as will be seen in the proposed mechanism. Furthermore at 0.01 M copper, the NiYCu species is formed to the extent of only a few per cent and cannot be responsible for the kinetic changes in this region.

Proposed Mechanism. A reaction mechanism is needed that accounts for the change in reaction order at pH 4.5, that accounts for the pH sensitivity, that agrees with the ionic strength effects, and that is consistent with the observable NiYCu species. Not only must the mechanism meet these requirements but it must also be consistent with a considerable body of other data for nickel-EDTA and other metal-multidentate ligand exchange reactions.^{1-3,5,6} Thus

(1) EDTA may completely dissociate from its metal complex before reacting with another metal. This occurs at high acidity and low concentration of the reacting metal. In the case of nickel, acid catalyzes the complete dissociation with the following rate expression^{17,18} at 1.25 μ and 25°

$$\frac{-d[\text{NiYT}]}{dt} = k_d^{\text{NiY}}[\text{NiYT}] \quad (13)$$

and for k_d^{NiY} in sec.^{-1}

$$k_d^{\text{NiY}}[\text{NiYT}] = 8 \times 10^4 [\text{H}^+][\text{NiY}^{-2}] + 2.0 \times 10^{-3} [\text{H}^+] \times [\text{NiYH}^-] + 0.21 [\text{H}^+]^2 [\text{NiYH}^-] + 1.0 [\text{H}^+]^3 [\text{NiYH}^-] \quad (14)$$

However, at very high acidity (*i.e.*, 0.7 M HCl) the rate of dissociation appears to reach a limiting value.^{18a} Unless the pH is very low, the complete acid dissociation of nickel-EDTA is too slow a process to account for any of the observed reaction rates with copper.

(2) A comparison of the EDTA-metal exchange reactions with hydroxyethylethylenediaminetriacetate complexes⁵ and with *trans*-cyclohexylenediaminetetraacetate complexes⁶ indicates the importance of dinuclear reaction intermediates with an iminodiacetate segment of EDTA associated with each metal ion.

(3) The relative rates of reaction of Fe^{+3} , Zn^{+2} , Ni^{+2} , Cu^{+2} , and H^+ with nickel-EDTA fit a mechanism with an iminodiacetate segment of EDTA bound to the incoming metal ion. A plot of $\log k_M^{\text{NiY}}$ against $\log K_{\text{M(iminodiacetate)}}$ gives a straight line with slope of unity.³ This supports the proposal that Ni-EDTA-M has one nitrogen bonded to nickel and one to M in the reaction intermediate proceeding the rate-determining cleavage of nickel from its segment of EDTA. (Alternatively the dinuclear structure must be a transition state closer to the products than reactants.)

(4) The reaction of copper with nitrilotriacetato-nickelate(II)¹³ gives comparable kinetic data which

(17) C. M. Cook, Jr., and F. A. Long, *J. Am. Chem. Soc.*, **80**, 33 (1958).

(18) (a) J. F. G. Clarke, Jr., M.S. Thesis, Purdue University, 1958;

(b) D. W. Margerum, *J. Phys. Chem.*, **63**, 336 (1959).

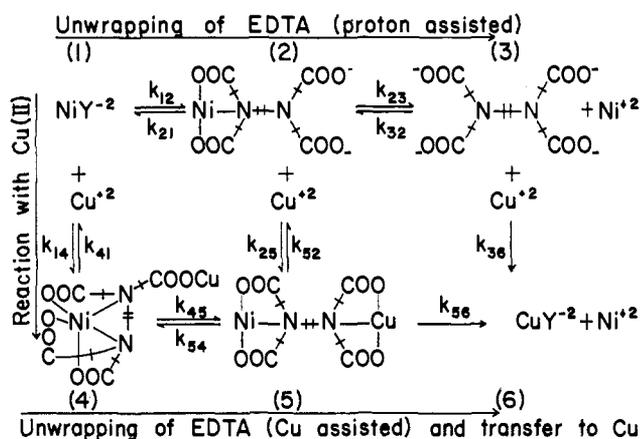


Figure 7. Stepwise unwrapping of EDTA from its nickel complex and the formation of the copper-EDTA complex. Only species 1, 4, 6, and protonated forms of 3 are observable intermediates. Species 2 and 5 are proposed reaction intermediates.

must be consistent with the proposed mechanism for copper and nickel-EDTA.

(5) The rate constant for Cu^{+2} and HY^{-3} is $1.3 \times 10^9 \text{ M}^{-1} \text{ sec.}^{-1}$ at 25° and 0.1 μ .^{19,20} In general, the rates of substitution reactions with $\text{Cu}^{+2}(\text{aq})$ are very fast, corresponding to what is believed to be the first-order rate constant for loss of water from copper²¹ equal to $3.0 \times 10^8 \text{ sec.}^{-1}$. The corresponding rate constant for the aquo nickel ion equals $2 \times 10^4 \text{ sec.}^{-1}$. However, when nickel is complexed with an iminodiacetate group, the rate constant for loss of water is increased²² to approximately $7 \times 10^4 \text{ sec.}^{-1}$.

In Figure 7 a mechanism is outlined which is consistent with all the above points. Protons are omitted from the reaction scheme for the sake of simplicity but several steps including the rate constants k_{12} and k_{23} are proton assisted. Step 1,2 and step 2,3 are not affected by copper while step 4,5 and step 5,6 are copper assisted. The location of the rate-determining step in this mechanism dictates the dependence of the reaction order on copper. However, the great lability of the aquo copper ion to substitution reactions compared to the more sluggish aquo nickel ion means that none of the steps involving k_{14} , k_{25} , or k_{36} should be rate determining.

When $[\text{H}^+] \gg [\text{Cu}^{+2}]$, the reaction proceeds by path 1,2,3,6 (or stops after step 2,3). The rate-determining reaction is step 2,3 as expressed by eq. 14. Only when $[\text{H}^+]$ is greater than 0.5 M does a limiting rate appear which suggests a shift to step 1,2 as the rate-determining step.

Above pH 2, path 1,2,3,6 does not contribute significantly to the rate of the reaction with copper. Two paths remain, both of which proceed through the unfolded dinuclear EDTA intermediate in species 5. A general kinetic expression for the reaction can then be written.

General Kinetic Expression. Neglecting path 2,3,6 and using steady-state approximations for species 2

(19) D. W. Margerum and B. A. Zabin, to be published.

(20) (a) K. Kato, *Bull. Chem. Soc. Japan*, **33**, 600 (1960); (b) H. Ackermann and G. Schwarzenbach, *Helv. Chim. Acta*, **35**, 485 (1952).

(21) M. Eigen, *Pure Appl. Chem.*, **6**, 97 (1963).

(22) D. W. Margerum and M. Eigen, "Proceedings of the 8th International Conference on Coordination Chemistry," Springer-Verlag, Vienna, 1964, p. 289.

and 5 and assuming rapid equilibration between species 1 and 4 ($K_{41} = k_{14}/k_{41}$) gives the expression for the observed first-order rate constant in eq. 15.

$k_o =$

$$\left(\frac{[k_{12}k_{25} + k_{45}K_{41}(k_{21} + k_{25}[\text{Cu}^{+2}])]k_{56}}{k_{21}(k_{56} + k_{52} + k_{54}) + k_{25}(k_{56} + k_{54})[\text{Cu}^{+2}]} \right) \times \left(\frac{[\text{Cu}^{+2}]}{1 + K_{41}[\text{Cu}^{+2}]} \right) \quad (15)$$

Case A. When the concentration of copper ion is low or if copper and hydrogen ion are the same order of magnitude the expression in eq. 15 can be simplified. For example, consider the situation where $[\text{Cu}^{+2}] = 10^{-4}$ to 10^{-5} M and pH 4 to 5.

(a) $1 \gg K_{41}[\text{Cu}^{+2}]$, because $K_{41} = 6.8$ at $\mu = 1.25$.

(b) $k_{52} \gg k_{56} + k_{54}$, because k_{52} involves the reaction of the more labile copper ion while both k_{56} and k_{54} involve substitution of the much more sluggish nickel ion. In addition $k_{56} \gg k_{54}$ because step 5,4 involves the prior dissociation of copper from a glycine group followed by the coordination of the group to nickel, while step 5,6 involves only nickel dissociation. Hydrogen ion would be expected to assist step 5,6 but not step 5,4.

(c) $k_{12}k_{25}/k_{21} \gg K_{41}k_{45}$, because $k_{25}/k_{21} \cong 10^3 \gg K_{41}$ and because k_{12} and k_{45} are of the same order of magnitude (compare lines B and D in Figure 1).

(d) $k_{21}(k_{56} + k_{52} + k_{54}) \gg k_{25}(k_{56} + k_{54})[\text{Cu}^{+2}]$, as in (b) above.

These simplifications give as the first-order rate constant

$$k_o = \frac{k_{12}k_{25}}{k_{21}k_{52}} k_{56} [\text{Cu}^{+2}] \quad (16)$$

or as defined in eq. 5 a second-order rate constant

$$k_{\text{Cu}^{\text{NiY}}} = \frac{k_{12}k_{25}}{k_{21}k_{52}} k_{56} \quad (17)$$

Equations 16 and 17 hold for individual runs under the conditions specified. Table II shows that a tenfold

Table II. Constancy of $k_{\text{Cu}^{\text{NiY}}}$ with Changes of Copper Concentration under Conditions of Case A

μ	$[\text{Cu}^{+2}], M$	$[\text{NiY}^{-2}], M$	pH	$k_{\text{Cu}^{\text{NiY}}}, M^{-1} \text{sec.}^{-1}$
0.10	1.59×10^{-5}	1.59×10^{-5}	5.64	0.12
			5.70	0.12
	1.50×10^{-4}	1.50×10^{-4}	5.60	0.11
			5.70	0.11
1.25	9.75×10^{-3}	9.95×10^{-3}	4.30	0.075 ^a
			4.64	0.078 ^a
	4.40×10^{-3}	2.29×10^{-3}	3.40	0.017
			2.90	0.017
6.60×10^{-3}	7.62×10^{-3}	3.15	0.017	
		2.20	0.016	

^a Figure 10 indicates why these $k_{\text{Cu}^{\text{NiY}}}$ values at 0.1 μ are not the same at pH 4.6 and 5.6.

change of $[\text{Cu}^{+2}]$ gives the same value for $k_{\text{Cu}^{\text{NiY}}}$. However, because the assumption in (d) skirts the borderline of validity, even at 10^{-4} M copper, $k_{\text{Cu}^{\text{NiY}}}$

is more accurately determined from an extrapolation after observing the effect of increased copper.

Equations 16 and 17 also hold at much higher copper concentrations if the hydrogen ion concentration is higher (Table II). This is understandable from the general rate expression because as $[\text{H}^+]$ is increased, the value of k_{12} is increased and the value of k_{21} is decreased. This would be expected in that a proton would help the half-dissociation, and the presence of protonated forms of species 2 would diminish the reverse rate constant. In a similar manner, protons should diminish the value of k_{25} , but increase the values of k_{52} and k_{56} . As a result, eq. 15 again simplifies to eq. 17. Furthermore, at low pH, path 1,4,5,6 is not important because H^+ competes with Cu^{+2} to form mixed complexes such as NiYH^- and NiYH_2 , and there is less of species 4.

Case B. When the concentration of copper is 10^{-4} to 10^{-2} M at pH 3-5, a transition in reaction order takes place. Using the general rate expression and the assumption that $k_{52} \gg k_{56} + k_{54}$ and $k_{56} > k_{54}$ permits eq. 18 to be written from eq. 15.

$$\left[1 + \frac{k_{45} K_{41} \left(\frac{k_{21}}{k_{25}} + [\text{Cu}^{+2}] \right)}{1 + K_{41}[\text{Cu}^{+2}]} \right] \times \frac{[\text{Cu}^{+2}]}{k_o} = \frac{1}{k_{\text{Cu}^{\text{NiY}}}} + \frac{1}{k_{12}} [\text{Cu}^{+2}] \quad (18)$$

Under the conditions specified with appropriate estimates of the constants, it can be shown that the expression within the brackets on the left-hand side of eq. 18 equals to within a few per cent of unity. Thus, eq. 19 has exactly the same form as eq. 7. The slopes

$$\frac{1}{k} = \frac{[\text{Cu}^{+2}]}{k_o} = \frac{1}{k_{\text{Cu}^{\text{NiY}}}} + \frac{1}{k_{12}} [\text{Cu}^{+2}] \quad (19)$$

of the lines in Figure 3 correspond to $1/k_{12}$ and their intercepts to $1/k_{\text{Cu}^{\text{NiY}}}$. Table III gives the values of

Table III. Ionic Strength Effect on $k_{\text{Cu}^{\text{NiY}}}$ and k_{12}

μ	pH	$k_{\text{Cu}^{\text{NiY}}}, M^{-1} \text{sec.}^{-1}$	$k_{12}, \text{sec.}^{-1}$
1.25	4.5 ± 0.1	2.1×10^{-2}	1.6×10^{-4}
0.80	4.8 ± 0.1	2×10^{-2}	1.6×10^{-4}
0.40	4.5 ± 0.1	3.7×10^{-2}	2.4×10^{-4}
0.10	4.5 ± 0.1	7.1×10^{-2}	3.8×10^{-4}

these constants at different ionic strengths. At pH 4.5 the major reactants are NiY^{-2} and Cu^{+2} , so that the ionic strength effect on $k_{\text{Cu}^{\text{NiY}}}$ fits the mechanism. The rate constant k_{12} does not depend on Cu^{+2} and the effect of ionic strength is less. If k_{12} were a true first-order constant the ionic strength should have even less effect. Whereas the $k_{\text{Cu}^{\text{NiY}}}$ values are relatively pH insensitive below pH 5, this is not the case with k_{12} . As will be seen, k_{12} is a pseudo-first-order rate constant because it depends on $[\text{H}^+]$, and therefore k_{12} decreases as the ionic strength increases.

Step 1,2 in the reaction mechanism corresponds to the unwrapping of an iminodiacetate segment of EDTA

from nickel. As the copper concentration in the solution increases, the relative concentration of species 5 increases and the rate increases. This is easily seen from the steady-state approximation for species 5 which gives

$$\frac{[5]}{[2]} = \frac{k_{25}[Cu^{+2}]}{k_{56} + k_{52}}$$

This continues until the reaction progress becomes limited by the rate at which species 2 is formed. The reaction rate then no longer increases with an increase in copper. Thus, the rate-determining step shifts from step 5,6 to step 1,2 as a function of copper ion concentration. Neither species 2 nor 5 is found in measurable concentration in solution but both are reaction intermediates. This accounts for the behavior observed in Figure 2 and for the transition from line A to line B in Figure 1.

Case C. From 10^{-2} to $0.3 M$ copper and low $[H^+]$ the expression for the observed rate constant is given in eq. 20. At pH 4.5 and $\mu = 1.25$, all the constants in

$$k_0 = \left(\frac{1 + \frac{k_{45}}{k_{12}} K_{41}[Cu^{+2}]}{1 + K_{41}[Cu^{+2}]} \right) \frac{k_{12} k_{Cu^{NiY}} [Cu^{+2}]}{k_{12} + k_{Cu^{NiY}} [Cu^{+2}]} \quad (20)$$

this expression except k_{45} are known. The value of k_{45} was estimated from the average value of k_0 for the two points near $0.22 M Cu^{+2}$. This gives $k_{45} \cong 35 \times 10^{-5} \text{ sec.}^{-1}$, and the curve fitting the points above $0.01 M Cu^{+2}$ at pH 4.5 in Figure 1 is drawn to fit eq. 21 with the values of k_{12} , k_{45} , K_{41} , and $k_{Cu^{NiY}}$ as specified.

The scatter of the data at high copper concentrations is due in part to the difficulty in adjusting the solutions to exactly pH 4.5 because of the ease of copper hydroxide precipitation.

According to the proposed mechanism, line C in Figure 1 does not represent a true first-order copper region but is actually the transition between two zero-order regions (k_{12} to k_{45}).

Case D. At very high copper and low $[H^+]$ the value of $K_{41}[Cu^{+2}]$ is greater than unity, and in theory essentially all the reactants could be in the form of species 4. Under these conditions

$$k_0 = k_{45} \quad (21)$$

and this represents the upper limit of the observed rate constant as the copper ion concentration increases. This limit should not be reached until the copper ion concentration considerably exceeds $1 M$ because $K_{41} = K_{NiYCu} = 6.8$. This cannot be tested at $\mu = 1.25$ or at pH 4.5, but it is apparent from the data in Figure 1 that the rate constant is approaching a new plateau at high copper concentrations. Line D corresponds to eq. 21. Actually, k_{45} will establish this plateau only if it is greater than k_{12} . This is the case at pH 4.5 but not at pH 3.3 where the acid-catalyzed k_{12} term apparently predominates.

Hydrogen Ion Effect on k_{12} . The value of k_{12} was determined for a variety of pH values at ionic strengths of 0.40 and 0.10 M . In addition to the points in Figure 3, the data given in Tables IV and V were used

Table IV. Effect of Acidity on the First-Order Rate Constant for the Half-Unwrapping of EDTA from Nickel^a

pH	$[NiY^{-2}], M$	$k_0, \text{sec.}^{-1}$	$k_{12}, \text{sec.}^{-1b}$
4.52	1.03×10^{-8}	2.15×10^{-4}	2.9×10^{-4}
4.54		2.07×10^{-4}	2.8×10^{-4}
4.63	8.28×10^{-4}	1.85×10^{-4}	2.4×10^{-4}
4.68		1.69×10^{-4}	2.1×10^{-4}
4.80		1.50×10^{-4}	1.8×10^{-4}
4.88		1.52×10^{-4}	1.8×10^{-4}
5.14		1.49×10^{-4}	1.8×10^{-4}
5.17		1.47×10^{-4}	1.8×10^{-4}
5.21		1.30×10^{-4}	1.6×10^{-4}
5.22		1.24×10^{-4}	1.5×10^{-4}

^a $[Cu^{+2}] = 0.025 M, 25.0^\circ, \mu = 0.4$. ^b To determine k_{12} values, the intercepts of plots of $1/k$ against (Cu^{+2}) were assumed to be the same as that of Figure 3 ($30 M \text{ sec.}$). Additional evidence for this contention is to be found in Table I (runs with low copper, $\mu = 0.4$).

Table V. Rate Constants Used to Calculate k_{12} at Different Ionic Strengths and Acidities

μ	pH	$[Cu^{+2}], M$	$k, M^{-1} \text{sec.}^{-1}$	$k_{12}, \text{sec.}^{-1}$
0.1	5.37	5.68×10^{-8}	1.8×10^{-2}	2.7×10^{-4}
	5.29	7.95×10^{-8}	1.6×10^{-2}	
	5.28	1.02×10^{-2}	1.4×10^{-2}	
	5.10	1.02×10^{-2}	1.6×10^{-2}	
	5.12	3.40×10^{-8}	2.8×10^{-2}	
	4.67	1.2×10^{-8}	5.5×10^{-2}	
	4.65	9.75×10^{-8}	2.3×10^{-2}	
1.25	4.05	5.06×10^{-2}	9.3×10^{-3}	5.7×10^{-4}
	4.96	2.14×10^{-2}	3.2×10^{-3}	0.8×10^{-4}
	4.64	3.99×10^{-2}	3.7×10^{-3}	
	4.62	4.99×10^{-2}	3.4×10^{-3}	
	4.64	5.35×10^{-2}	3.1×10^{-3}	
	3.27	9.75×10^{-8}	1.5×10^{-2}	
	3.32	4.88×10^{-2}	9.1×10^{-3}	
			8.8×10^{-4}	

to evaluate k_{12} at different acidities and ionic strengths. Figures 8 and 9 show plots of k_{12} values (obtained in some cases by assuming linear resolution of the data in accord with eq. 19) against $[H^+]$. Over the pH range 4.0 to 5.2, eq. 22 appears to be valid, where $k_d^{NiY^{-1/2}}$

$$k_{12} = k_d^{NiY^{-1/2}} + k_H^{NiY^{-1/2}}[H^+] \quad (22)$$

is the dissociation rate constant for the half-unwrapping of EDTA from nickel and $k_H^{NiY^{-1/2}}$ is that for the proton-assisted half-unwrapping.

In a similar manner these constants were estimated from the data in Table V for 1.25 M ionic strength. The proton and nonproton dependent rate constants for the half-unwrapping of EDTA from nickel are summarized in Table VI.

Table VI. Proton-Dependent and Nonproton-Dependent Rate Constants for the Half-Unwrapping of EDTA from Nickel

μ	$k_d^{NiY^{-1/2}}, \text{sec.}^{-1}$	$k_H^{NiY^{-1/2}}, M^{-1} \text{sec.}^{-1}$
1.25	1×10^{-4}	2.2
0.40	1.3×10^{-4}	4.7
0.10	2.2×10^{-4}	6.9

A value for $k_d^{NiY^{-1/2}}$ can be calculated from the proposed mechanism in Figure 7. Assuming no H^+

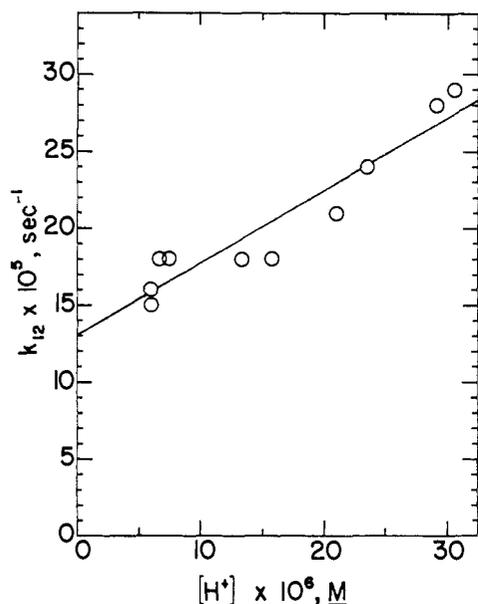


Figure 8. Resolution of k_{12} into proton-dependent and nonproton-dependent terms (25.0°, $\mu = 0.4$, $[\text{Cu}^{2+}] = 0.025 \text{ M}$); values of k_{12} determined by assuming same intercept as in Figure 3.

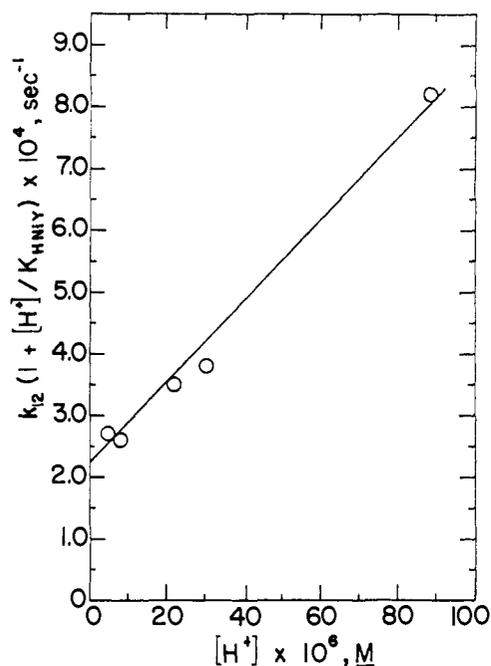


Figure 9. Resolution of k_{12} into proton-dependent and nonproton-dependent terms (25.0°, $\mu = 0.10$); values of k_{12} from Figure 3 and Table V.

catalysis, $k_{12} = k_d^{\text{NiY}^{-1/2}}$ and

$$\frac{k_{12}}{k_{21}} = \frac{K_{\text{NiIDA}}}{K_{\text{NiY}}} \times \text{electrostatic factor} \quad (23)$$

The electrostatic factor arises from the net attraction the remote negative groups have for the positive nickel—the repulsion they have for each other is inherent in their structure and does not affect the stability of the nickel complex. The electrostatic factor of 50 can be estimated using a distance of 7 Å. and the dielectric constant for water. In addition there is a statistical factor of either 2 or $1/2$ depending on whether EDTA is

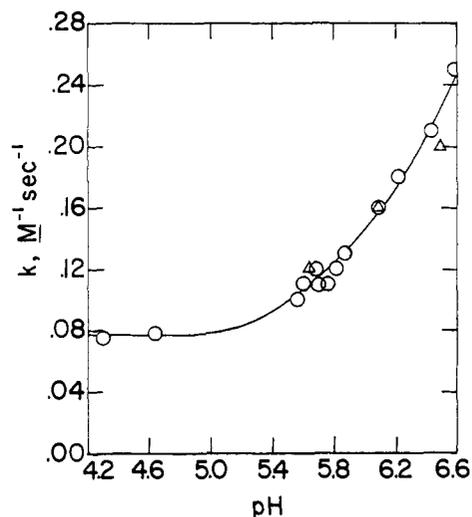


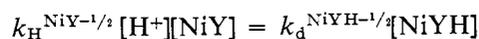
Figure 10. pH profile of observed second-order rate constant (25.0°, $\mu = 0.10$): Δ , 10^{-5} M reactants; \circ , 10^{-4} M reactants.

five- or six-coordinated. This factor is omitted from the calculation. The value for k_{21} can be considered equal to the rate of loss of water from nickel iminodiacetate which has been estimated to be $7 \times 10^4 \text{ sec}^{-1}$.²² As a result the predicted value for $\mu = 0.1$ using methyl iminodiacetate as the model is given in eq. 24. Table calcd. $k_d^{\text{NiY}^{-1/2}} =$

$$\frac{10^{8.7}}{10^{18.6}} \times 50 \times 7 \times 10^4 \cong 4 \times 10^{-4} \text{ sec}^{-1} \quad (24)$$

VI shows the experimental value at 0.1 μ to be $2.2 \times 10^{-4} \text{ sec}^{-1}$, which is in good agreement with the calculated value.

Hydrogen ion is much more effective than Cu^{2+} in assisting the half-opening of EDTA from nickel. One reason is that the H^+ complex is stronger as shown in eq. 11. However, even after NiYCu has formed it is only about $1/7$ as effective as NiYH^- in causing the half-opening.



at 1.25 μ

$$k_d^{\text{NiYH}^{-1/2}} = k_{\text{H}}^{\text{NiY}^{-1/2}} \frac{[\text{H}^+][\text{NiY}]}{[\text{HNiY}]} = 2.6 \times 10^{-3} \text{ sec}^{-1}$$

while

$$k_{45} \cong k_d^{\text{NiYCu}^{-1/2}} = 0.35 \times 10^{-3}$$

This suggests that H^+ plays a larger role than simply protonating a free carboxylate group in nickel-EDTA. Perhaps the proton assists the first nickel-nitrogen bond cleavage in some way not possible for copper. At much higher concentrations, proton assistance of the first Ni-N bond cleavage in the ethylenediamine complex of nickel is reported.⁷

Hydroxide Ion Effect. Figure 10 is a pH profile of the second-order rate constant, k (see eq. 4), at $\mu = 0.10$ where the reactants are 10^{-4} or 10^{-5} M . The value of k at pH 4.2 and 4.65 corresponds approximately to the value of $k_{\text{Cu}^{\text{NiY}}}$, but as the pH increases from 5.6 to 6.6 there is a threefold increase in the rate of the reaction. This cannot be attributed to

changes in nickel-EDTA because there is less than 0.1% NiHY⁻ above pH 6 and less than 10⁻⁵% NiYOH⁻ below pH 7. The formation of a complex with hydroxide bound to copper in species 5 is thought to cause the acceleration in rate.

A more detailed examination of the hydroxide effect on copper(II) in ligand-exchange reactions will be given in subsequent papers.

Conclusions

The reaction between copper and nickel-EDTA appeared at first to be a kinetic maze—three apparent changes of reaction order with copper concentration and a pH dependence sometimes present and sometimes not. However, the very complexity of the kinetics imposes restrictions upon the possible explanations of the behavior at each condition. This, in turn, means increased confidence in any mechanism that can fit all the data. All the complexities can be unravelled both qualitatively and quantitatively by the consideration of a simple step-by-step mechanism of unwrapping EDTA from nickel and wrapping it around copper. Figure 7 represents an abbreviated form of this stepwise procedure, showing some of the combined steps which could be identified. In multidentate ligand exchange reactions an analysis of the possible reaction intermediates is helpful in understanding not only the effect of changes of ligand structure^{6,6} but also the effect of different metal ions on the reaction rate. In addition, as in this case, a consideration of the possible step-by-step reaction intermediates may be essential to the understanding of the kinetics of a single exchange reaction.

Analysis of Stepwise Mechanisms. The keys to the unravelling of multidentate ligand-exchange kinetics are relatively simple.

(1) Just as individual ligands have a stepwise series of stability constants with a metal, so the path of a multidentate ligand exchange reaction proceeds stepwise. In each step, solvent or another ligand replaces or is replaced by a dentate group of the multidentate ligand. In the case of transition metal ions and the aminocarboxylate ligands, the making or breaking of the metal-nitrogen bonds are the most important kinetic steps.

(2) The stability of each reaction intermediate relative to the reactants can be estimated from the stability constant of the coordination segments and the electrostatic attraction or repulsion of the different ligands.

(3) The reaction rate constant for an individual step in the mechanism can be estimated from the exchange rate constant of the aquo metal ion and the stability constant of the coordinated segment. The substitution reactions for many monodentate octahedral complexes have been shown to be governed by a first-order dissociation process.²³ Therefore

$$k_M^{-L} = \frac{k_M^{-H_2O}}{K_{ML}} \quad (25)$$

(23) M. Eigen and R. G. Wilkins, "Mechanisms of Inorganic Reactions," Summer Symposium, Division of Inorganic Chemistry, American Chemical Society, Lawrence, Kan., June 1964.

There are, however, at least three stumbling blocks in applying these points to a mechanism. One concerns steric factors which may be of great importance as in the case of the *trans*-cyclohexylenediaminetetraacetate exchange reactions.⁶ More experimental information is needed about steric effects, but in the meantime, molecular models are helpful in estimating whether or not the steric effects can be expected to be important.

A second difficulty is that little is known about the effect of coordinated ligands on the rate of exchange of other ligands. The ratio of $k_{ML}^{-H_2O}/k_M^{-H_2O}$ may change with the structure of L (or segment of L which remains bonded). In the present case data were available for the effect of aminocarboxylate ligands on the substitution reactions of nickel.²¹ We are presently studying similar effects with other metal ions.

The third difficulty concerns the calculation of the effect of electrostatic repulsion on the stability of the intermediates and on the dissociation rate constants. The problem concerns the choice of the effective dielectric constant when the distance between charges is small. In the reactions of EDTA and its derivatives, repulsion between metals along the bond sequence M-N-C-C-N-M seems to be particularly important. However, electrostatic repulsion acts in an opposite direction on the stability constant and on the rate constant. As a result the product, $K_{intermediate}k_d$, for the rate-determining step is the same as that estimated by ignoring the electrostatic repulsion. This can be seen from eq. 25. If the value of K_{ML} is lowered, then k_M^{-L} must be increased proportionally.

In summary, despite some difficulties which presently prevent an exact evaluation of the relative importance of each step in multidentate ligand exchange reactions, there are sufficient facts known to make it profitable to analyze the possible mechanisms in terms of the stabilities of bonded segments and the rate constants for the loss of water from the aquo metal ions. The mechanism proposed in Figure 7 has been analyzed in these terms. The change in reaction order along the path 1,2,5,6 occurs because at higher copper concentrations the rate is sufficiently fast that the copper ion must wait for the nickel-EDTA to unwrap and present a free nitrogen group. Under these conditions, the acidity is very significant because it in turn determines how rapidly the nickel-EDTA half unwraps. On the other hand, at low copper concentration, the path 2,5,6 is not fast relative to step 1,2 and the rate depends upon the copper concentration. In the latter case the rate has relatively little acid dependence because any protons which assist the unwrapping also repel the copper.

Electrostatic Repulsion in Dinuclear Intermediates. In previous work²⁴ the importance of electrostatic repulsion between nickel in its reaction with protonated polyamines was discussed. For the dissociation of nickel polyamine complexes it was possible to assume that a charge on one part did not affect the remaining Ni-N bond dissociation rate constants. However, in most of these cases the proton was not on the nitrogen adjacent to that bonded to Ni. When the proton is adjacent (a distance of about 6 Å.), there does appear

(24) D. W. Margerum, D. B. Rorabacher, and J. F. G. Clarke, Jr., *Inorg. Chem.*, **2**, 667 (1963).

to be a measurable increase in the Ni-N bond cleavage rate constant.²⁵

Species 5 in Figure 7 has the same groups dissociating from nickel as species 1, but k_{56} must be much larger than k_{12} . This has to be the case because the limiting rate becomes $k_{12}[\text{NiY}^{-2}]$ at high copper (neglecting path 1,4,5) but the over-all rate also equals $k_{56}[5]$.

$$\text{rate} = k_{12}[\text{NiY}^{-2}] = k_{56}[5]$$

Since $[5] \ll [\text{NiY}^{-2}]$, then obviously $k_{56} \gg k_{12}$.

The experimental value of k_{12} corresponds closely to the calculated value based on the stabilities of species 1 and 2 and the rate constant for water substitution. If k_{56} is estimated in the same manner it would be slightly less than k_{12} , but this neglects electrostatic repulsion between copper and nickel which must be sufficiently large to make $k_{56} \gg k_{12}$. Such a repulsion along Ni-N-C-C-N-Cu would serve to weaken the Ni-N bond resulting in faster cleavage of this segment. Of course, the repulsion would weaken the Cu-N bond as well. Indeed the stability of the intermediate species 5 must be less than that calculated from the stabilities of the segments, otherwise species 5 would be observable at high copper concentrations and it is not. The term for the electrostatic repulsion between the two metal iminodiacetate segments in 5 must be greater than 10^2 .

Predictions for Other EDTA-Exchange Reactions. It is only fair to ask under what conditions the simple rate expression in eq. 2 will hold for other EDTA-

(25) G. A. Melson and R. G. Wilkins, *J. Chem. Soc.*, 2662 (1963).

exchange reactions. An evaluation of the constants in a stepwise mechanism for the EDTA exchange with other metals indicates that deviations from eq. 2 as the concentration of M' is increased up to 1 M should be expected if $K_{M'IDA}/K_{MIDA} > 1$ and if $k_{M'-\text{H}_2\text{O}}/k_{M-\text{H}_2\text{O}} > 1$. This situation occurs for a number of cases with Cu(II) reactions because copper forms a very stable iminodiacetate complex ($\log K = 10.6$) and also has rapid water substitution. Thus the reactions of Cu^{+2} and MgY^{-2} , Cu^{+2} and CoY^{-2} , Cu^{+2} and CdY^{-2} , and Cu^{+2} and AlY^{-} could all show the same type of deviations found for Cu^{+2} and NiY^{-2} . There are other combinations such as Zn^{+2} and MgY^{-2} which would be predicted to act similarly. Many of the reactions with copper have been studied, but because they are fairly rapid the copper concentration has been around $10^{-4} M$ and hence has been too low to cause the shift to step 1,2.

On the other hand, the reaction of Zn^{+2} and NiY^{-2} would not be expected to deviate from eq. 2, and this was the case up to at least 0.4 M Zn^{+2} at pH 5.

The position of the rate-determining step in multi-dentate ligand exchange reactions can, in general, be expected to shift with concentrations of metal ions and hydrogen ion. This can lead to complex changes in reaction order and makes extrapolation of reaction rate data from one concentration level to another dangerous unless the full mechanism is considered.

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Some Exchange and Substitution Reactions of Hexachlororhodium(III) and Pentachloroaquorhodium(III) Ions in Aqueous Acid Solutions

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This paper reports an extension of previous studies in this laboratory of the chemistry of rhodium(III) complexes. The present work comprises an investigation of the kinetics of the equilibration $\text{RhCl}_6^{-3} + \text{H}_2\text{O} \rightleftharpoons \text{RhCl}_5\text{H}_2\text{O}^{-2} + \text{Cl}^-$ (1) utilizing spectrophotometric and isotopic tracer techniques. The reaction was studied in perchloric-hydrochloric acid media of constant ionic strength. The aquation of RhCl_6^{-3} and the anation of $\text{RhCl}_5\text{H}_2\text{O}^{-2}$ were examined independently by spectrophotometry. It was shown that either process is described by the rate law

$$-d(\text{RhCl}_6^{-3})/dt = k_1(\text{RhCl}_6^{-3}) - k_2(\text{RhCl}_5\text{H}_2\text{O}^{-2})(\text{Cl}^-)$$

Values of k_1 and k_2 were obtained at several temperatures by both aquation and anation procedure, and excellent agreement was obtained between the two sets of data. At 25°, $k_1 = 0.11 \text{ min.}^{-1}$ and $k_2 = 0.013 M^{-1} \text{ min.}^{-1}$.

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The Arrhenius energies of activation are 25 and 17 kcal./mole, respectively. The reaction is essentially independent of acid concentration up to 4 M . In order to test whether the aquation path is the only one available for exchange of chloride by chloride, a direct study was made of the reaction $\text{RhCl}_6^{-3} + {}^{36}\text{Cl}^- \rightleftharpoons \text{RhCl}_5{}^{36}\text{Cl}^{-2} + \text{Cl}^-$. The kinetics of the isotopic exchange can be accounted for entirely by an aquation mechanism, according to reaction 1 and the succeeding aquation $\text{RhCl}_5\text{H}_2\text{O}^{-2} + \text{H}_2\text{O} \rightleftharpoons \text{RhCl}_4(\text{H}_2\text{O})_2^{-} + \text{Cl}^-$. Unfortunately, no conclusions can be drawn concerning the detailed mechanism of reaction 1. The forward process may involve a unimolecular dissociation of chloride ion as the rate-determining step, or bimolecular substitution of water for chloride. Since the reverse reaction seems to be a clear-cut bimolecular process (an ion-pairing mechanism is unlikely for ions of the same charge sign), it is quite possible that the aquation is also bimolecular in nature.