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Electron-Transfer Kinetics of the Reactions between Copper(III,II) and Nickel(III,II) Deprotonated-Peptide Complexes

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Electron-transfer rates for Cu(III) + Ni(II) ⇄ Cu(II) + Ni(III) are measured (32 in the forward and 13 in the reverse direction) for a series of deprotonated peptide complexes of copper and nickel. The reactions are relatively rapid, and various groups give excellent Marcus correlations. However, the fact that some of the reactions have enhanced electron-transfer rates while others are sterically hindered suggests an inner-sphere pathway. The degree of enhancement or steric hindrance depends on the nature of the peptide ligands.

Introduction

Copper(III) and nickel(III) deprotonated-peptide complexes, $Cu^{III}(H_{-n}L)$ and $Ni^{III}(H_{-m}L')$, are readily prepared by the chemical or electrochemical oxidation of the corresponding copper(II) or nickel(II) peptide and are moderately stable in aqueous media.[1-5] Electrochemical,[3,6,7] EPR,[8] and crystallographic[9-12] studies have shown that the d^7 nickel(III) and d^9 copper(II) complexes have tetragonally distorted octahedral geometries, while the d^8 nickel(II) and copper(III) complexes are square planar. The electron-transfer reactions between the copper(III) and nickel(II) peptides (eq 1, where n and m refer to the number of deprotonated peptide nitrogens) are

$$Cu^{III}(H_{-n}L) + Ni^{II}(H_{-m}L') + 4H_2O \rightleftarrows Cu^{II}(H_{-n}L)(H_2O)_2 + Ni^{III}(H_{-m}L')(H_2O)_2 \quad (1)$$

unusual in that they provide examples of one-electron transfers between two square-planar d^8 complexes (eq 1, Scheme I). The reverse reactions of copper(II) peptides oxidized by nickel(III) peptides exemplify one-electron transfers between complexes both of which have tetragonally distorted octahedral geometries. The relatively wide range of electrode potentials for the Cu(III,II) peptide couples[6] (Table I) facilitates the examination of the rates of these reactions as a function of free energy.

Originally, we had planned to use the copper–nickel electron-transfer reactions, together with the known self-exchange rate constants for copper(III,II) peptides,[13,14] to determine the self-exchange rate constants for the nickel(III,II) peptides. However, the values obtained from the copper–nickel reactions depend strongly on the nature of the peptide ligands, they differ from the self-exchange rate constants calculated from the nickel(III,II) peptide cross-reactions,[15] and they are much larger than recently determined outer-sphere nickel(III,II) peptide electron-transfer rate constants.[16] These results imply that the copper–nickel reactions follow inner-sphere or enhanced pathways rather than outer-sphere electron transfer. This work investigates the influence of peptide ligands on rates of copper(III,II)–nickel(III,II) electron-transfer reactions.

Scheme I

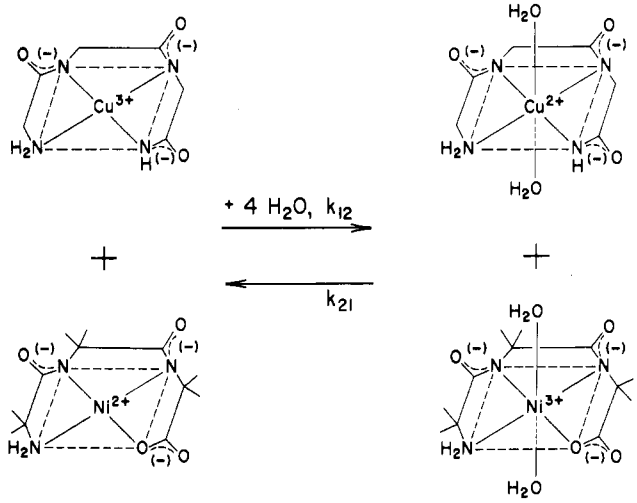

Table I. One-Electron Reduction Potentials for Some Copper(III)[a] and Nickel(III)[b] Deprotonated-Peptide Complexes (25.0 °C, μ = 0.10 ($NaClO_4$))

complex	$E^{\circ\prime}$, V (vs. NHE)	complex	$E^{\circ\prime}$, V (vs. NHE)
$Cu^{III}(H_{-3}Aib_3a)$	0.37[c]	$Cu^{III}(H_{-2}leu_3)$	0.77
$Cu^{III}(H_{-3}A_5)^-$	0.58[d]	$Cu^{III}(H_{-2}A_3)$	0.81
$Cu^{III}(H_{-3}PG_2a)$	0.60	$Cu^{III}(H_{-2}GA_2)$	0.85
$Cu^{III}(H_{-3}A_4)^-$	0.60	$Cu^{III}(H_{-2}G_2A)$	0.88
$Cu^{III}(H_{-3}G_2Aa)$	0.60	$Cu^{III}(H_{-2}G_3)$	0.92
$Cu^{III}(H_{-3}VG_2a)$	0.61	$Cu^{III}(H_{-3}G_2\beta A)$	0.94
$Cu^{III}(H_{-3}FGGa)$	0.62	$Ni^{III}(H_{-3}Aib_3a)$	0.815[g]
$Cu^{III}(H_{-3}G_4)^-$	0.63	$Ni^{III}(H_{-2}Aib_3)$	0.82[h]
$Cu^{III}(H_{-3}G_3a)$	0.64	$Ni^{III}(H_{-3}G_3a)$	0.83
$Cu^{III}(H_{-3}G_5)^-$	0.66	$Ni^{III}(H_{-3}FGGa)$	0.83[d]
$Cu^{III}(H_{-3}Aib_3)$	0.66[e]	$Ni^{III}(H_{-3}G_4a)$	0.84
$Cu^{III}(H_{-3}G_4a)$	0.68	$Ni^{III}(H_{-2}G_2A)$	0.85
$Cu^{III}(H_{-3}G_3AOCH_3)$	0.70[f]		

[a] Reference 6. [b] Reference 3. [c] Reference 14. [d] Czarnecki, J. J. Ph.D. Thesis, Purdue University, 1976. [e] Reference 5. [f] Reference 24. [g] Reference 15. [h] This work.

The solution pH for the reactions in eq 1 can be adjusted so that the acid dissociation of the copper(II) peptides is much more rapid than the oxidation of $Cu^{II}(H_{-n}L)$, the acid dissociation of $Ni^{II}(H_{-m}L')$, or the acid decomposition of $Cu^{III}(H_{-n}L)$.[17-20] Under such conditions, copper(III) peptides can

(1) Margerum, D. W.; Chellappa, K. L.; Bossu, F. P.; Burce, G. L. *J. Am. Chem. Soc.* **1975**, *97*, 6894.
(2) Bossu, F. P.; Margerum, D. W. *J. Am. Chem. Soc.* **1976**, *98*, 4003.
(3) Bossu, F. P.; Margerum, D. W. *Inorg. Chem.* **1977**, *16*, 1210.
(4) Neubecker, T. A.; Kirksey, S. T., Jr.; Chellappa, K. L.; Margerum, D. W. *Inorg. Chem.* **1979**, *18*, 444.
(5) Kirksey, S. T., Jr.; Neubecker, T. A.; Margerum, D. W. *J. Am. Chem. Soc.* **1979**, *101*, 1631.
(6) Bossu, F. P.; Chellappa, K. L.; Margerum, D. W. *J. Am. Chem. Soc.* **1977**, *99*, 2195.
(7) Youngblood, M. P.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 3068.
(8) Lappin, A. G.; Murray, C. K.; Margerum, D. W. *Inorg. Chem.* **1978**, *17*, 1630.
(9) Diaddario, L. L.; Robinson, W. R.; Margerum, D. W. *Inorg. Chem.* **1983**, *22*, 1021.
(10) Freeman, H. C.; Taylor, M. R. *Acta Crystallogr.* **1965**, *18*, 939.
(11) Freeman, H. C. *Adv. Protein Chem.* **1967**, *22*, 257.
(12) Blount, J. F.; Freeman, H. C.; Holland, R. V.; Milburn, G. . W. *J. Biol. Chem.* **1970**, *245*, 5177.
(13) Koval, C. A.; Margerum, D. W. *Inorg. Chem.* **1981**, *20*, 2311.
(14) Anast, J. M.; Hamburg, A. W.; Margerum, D. W. *Inorg. Chem.* **1983**, *22*, 2139.
(15) Murray, C. K.; Margerum, D. W. *Inorg. Chem.* **1983**, *22*, 463.
(16) Kumar, K.; Margerum, D. W., to be submitted for publication.
(17) Pagenkopf, G. K.; Margerum, D. W. *J. Am. Chem. Soc.* **1968**, *90*, 6963.
(18) Youngblood, M. P.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 3072.

0020-1669/84/1323-1345$01.50/0

be used as oxidants for thermodynamically unfavorable electron-transfer reactions between copper(III) and nickel(II) peptides.

Two properties of the Ni(III,II) peptides complicate the study of their redox reactions. Ni(III) peptides undergo intramolecular redox decompositions that are both acid and base catalyzed,[21] and the Ni(II) peptides participate in moderately rapid acid dissociation reactions.[20,22] In spite of these complicating factors, the kinetics of the nickel(II) complexes of tetraglycinamide and triglycinamide, $Ni^{II}(H_{-3}G_4a)^-$ and $Ni^{II}(H_{-3}G_3a)^-$, by a series of copper(III) complexes were investigated.

In marked contrast to the other nickel(III) peptides, the complex of di-α-aminoisobutyryl-α-aminoisobutyric acid, $Ni^{III}(H_{-2}Aib_3)$, possesses unusual kinetic stability and appears to be inert to peptide substitution, to acid attack, and to acid-catalyzed intramolecular redox decomposition.[5] The $Ni^{II}(H_{-2}Aib_3)^-$ complex also dissociates more slowly in acid than the other Ni(II) peptides. These properties make the $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ couple suitable for the study of Ni(III,II) electron-transfer reactions.

Experimental Section

Di-α-aminoisobutyryl-α-aminoisobutyric acid (Aib_3) was synthesized by the method of Kirksey.[5] Di-α-aminoisobutyryl-α-aminoisobutyric acid amide (Aib_3a) was synthesized by Hamburg.[23] The other peptides were purchased from Biosynthetika, Vega-Fox, or Cyclo Chemical Co. and used without a further purification. The abbreviations used for the amino acid residues (L isomers) are as follows: glycyl, G; alanyl, A; β-alanyl, βA; leucyl, leu; prolyl, P; valyl, V; phenylalanyl, F; G_3a is glycylglycylglycinamide, etc.

Millimolar solutions of Ni(II) peptide complexes were prepared by mixing solutions of $Ni(ClO_4)_2$ with a 5–10% excess of the peptide ligand and slowly raising the pH. In order to ensure complete formation of the fully deprotonated complexes, the pH was raised to 9.5 for the doubly deprotonated complexes and to 10.5 for the triple deprotonated complexes. The ionic strengths of the resulting solutions were adjusted with $NaClO_4$.

As in previous electron-transfer studies of copper peptides,[24-26] an ionic strength of 0.10 was used for reactions involving $Ni^{II}(H_{-2}G_2A)^-$, $Ni^{II}(H_{-2}Aib_3)^-$, or $Ni^{II}(H_{-3}Aib_3a)^-$. For reactions of $Ni^{II}(H_{-3}G_3a)^-$ or $Ni^{II}(H_{-3}G_4a)^-$, the ionic strength was maintained at 0.5 ($NaClO_4$ + NaOAc).

The nickel(III) peptide reagents were prepared by the electrolysis of Ni(II) peptide solutions using an electrochemical flow cell that contained a graphite working electrode.[27] Immediately prior to the oxidation of $Ni^{II}(H_{-2}Aib_3)^-$ or $Ni^{II}(H_{-3}Aib_3a)^-$, the pH of the solution was adjusted to pH 6.5–7, as the oxidation of these complexes in more basic solution can result in the generation of products other than $Ni^{III}(H_{-2}Aib_3)$ or $Ni^{III}(H_{-3}Aib_3a)$. The slow acid dissociation properties of $Ni^{II}(H_{-2}Aib_3)^-$ and $Ni^{II}(H_{-3}Aib_3a)^-$ make it possible to perform the pH adjustment without losing significant amounts of the fully deprotonated species. The stability of freshly oxidized $Ni^{III}(H_{-2}Aib_3)$ in 0.02 M buffer at pH 8 was examined by monitoring its absorbance at 350 nm. No loss of the complex was detected 5 min after mixing with the buffer. Solutions of $Ni^{III}(H_{-2}Aib_3)$ that had aged for more than 5 min at pH 8 were not used in the kinetic determinations.

Table II. Reduction Potential for $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ from Kinetic Measurements for a Series of $Cu^{III,II}(H_{-n}L)^{0,-}$ and $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ Redox Couples[a]

oxidant	$\Delta E^{\circ\prime}$, V (from k_{12}/k_{21})[b]	$E^{\circ\prime}$, V (for $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$)[c]
$Cu^{III}(H_{-2}A_3)$	−0.010	0.820
$Cu^{III}(H_{-2}leu_3)$	−0.040	0.810
$Cu^{III}(H_{-3}G_3AOCH_3)$	−0.102	0.802
$Cu^{III}(H_{-3}G_4a)$	−0.137	0.817
$Cu^{III}(H_{-3}G_3a)$	−0.175	0.815

[a] T = 25.0 °C, μ = 0.10. [b] For the reactions

$$Cu^{III}(H_{-n}L) + Ni^{II}(H_{-2}Aib_3)^- \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} Cu^{II}(H_{-n}L)^- + Ni^{III}(H_{-2}Aib_3)$$

(see Tables III and IV). [c] From $-\Delta E^{\circ\prime} + E^{\circ\prime}$ for the $Cu^{III,II}(H_{-n}L)^{0,-}$ couple (see Table I).

Millimolar solutions of the copper(II) peptides were prepared by mixing $Cu(ClO_4)_2$ with a 5–10% excess of the appropriate peptide and raising the pH to 9.5 for doubly deprotonated and to 10.5 for triply deprotonated complexes. The pK_a values for these complexes are such that fully deprotonated tripeptide complexes are formed above pH 9, while fully deprotonated tripeptide amide and tetrapeptide complexes are formed above pH 10.[28]

For reactions with $Ni^{III}(H_{-2}Aib_3)$ buffered with borate, the Cu(II) peptides were diluted ($(2–8) \times 10^{-4}$ M) with slightly basic 0.1 M $NaClO_4$. Alternatively, slightly acidic (pH 4.5–5) Ni(III) peptide solutions were allowed to react with Cu(II) peptides buffered with phosphate (pH 7.8–8). For reactions with the Ni(II) peptides, millimolar solutions of Cu(II) peptides were oxidized to the corresponding Cu(III) complexes with the electrochemical flow cell, and the Cu(III) peptides produced in this manner were diluted (2×10^{-5} M) with acetate buffer containing sufficient $NaClO_4$ to adjust the ionic strength to 0.1 for reactions with $Ni^{II}(H_{-2}Aib_3)^-$ and to 0.5 for reactions with $Ni^{II}(H_{-3}G_3a)^-$ or $Ni^{II}(H_{-3}G_4a)^-$.

The redox reactions were monitored with a computer-interfaced stopped-flow spectrophotometer[29] thermostated at 25.0 °C. For reactions of the Ni(II) peptides with Cu(III) peptides, the loss of Cu(III) was observed by monitoring the absorbance at 365 nm (tripeptide amides or tetrapeptides, $\epsilon \sim 7000$ M^{-1} cm^{-1}) or at 385–395 nm (tripeptide, $\epsilon \sim 5000$ M^{-1} cm^{-1}). For reactions of the Ni(III) peptides with an excess of the Cu(II) peptides, the formation of Cu(III) was monitored at 365 or 385–395 nm.

The acid dissociation of $Ni^{II}(H_{-2}Aib_3)^-$ was monitored at 410 nm ($\epsilon \sim 200$ M^{-1} cm^{-1}).

Results and Discussion

The $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ Reduction Potential. Measurements of the formal reduction potential, $E^{\circ\prime}$, of $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ by cyclic voltammetry have given values of 0.82,[30] 0.83,[15] and 0.84 V[5] vs. NHE. To help establish a value for this reduction potential the equilibrium in eq 2 was examined spectrophotometrically at pH 6.8. The measured absorbance at 490 nm was used to calculate the $IrCl_6^{2-}$ concentration ($\epsilon^{490} = 4075$ M^{-1} cm^{-1} for $IrCl_6^{2-}$),[31] while the concentration of $Ni^{III}(H_{-2}Aib_3)$ was determined from the absorbance at 352 nm ($\epsilon^{352} = 3600$ M^{-1} cm^{-1} for $Ni^{III}(H_{-2}Aib_3)$).[5] The spectrophotometric data and the known $Ir^{IV,III}Cl_6^{2-,3-}$ reduction potential of 0.892 V vs. NHE[1] gives a value of 0.814 (±0.004) V vs. NHE from the reaction of $Ni^{II}(H_{-2}Aib_3)^-$ with $IrCl_6^{2-}$, while the value obtained from the reverse reaction is 0.811 (±0.004) V.

$$Ni^{II}(H_{-2}Aib_3)^- + IrCl_6^{2-} \rightleftarrows Ni^{III}(H_{-2}Aib_3) + IrCl_6^{3-} \quad (2)$$

The reduction potential of $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ also may be calculated from the forward and reverse rate constants for

(19) Hauer, H.; Dukes, G. R.; Margerum, D. W. *J. Am. Chem. Soc.* **1973**, *95*, 3515.
(20) Raycheba, J. M. T.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 487.
(21) Bossu, F. P.; Paniago, E. B.; Margerum, D. W.; Kirksey, S. T., Jr.; Kurtz, J. L. *Inorg. Chem.* **1978**, *17*, 1034.
(22) Paniago, E. B.; Margerum, D. W. *J. Am. Chem. Soc.* **1972**, *94*, 6704.
(23) Hamburg, A. W.; Nemeth, M. T.; Margerum, D. W. *Inorg. Chem.* **1983**, *22*, 3535.
(24) Owens, G. W.; Chellappa, K. L.; Margerum, D. W. *Inorg. Chem.* **1979**, *18*, 960.
(25) DeKorte, J. M.; Owens, G. D.; Margerum, D. W.; *Inorg. Chem.* **1979**, *18*, 1538.
(26) Lappin, A. G.; Youngblood, M. P.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 407.
(27) Clark, B. R.; Evans, D. H. *J. Electroanal. Chem.* **1965**, *69*, 181.
(28) Margerum, D. W.; Wong, L. F.; Bossu, F. P.; Chellappa, K. L.; Czarnecki, J. J.; Kirksey, S. T., Jr.; Neubecker, T. A. *Adv. Chem. Ser.* **1977**, *No. 162*, 281.
(29) Willis, B. G.; Bittikofer, J. A.; Pardue, H. D.; Margerum, D. W. *Anal. Chem.* **1970**, *42*, 1340.
(30) Youngblood, M. P.; Margerum, D. W., unpublished results.
(31) Thorneley, R. N.; Sykes, A. G. *J. Chem. Soc. D* **1969**, 331.

electron-transfer reactions between $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ and $Cu^{III,II}(H_{-n}L)^{0,-}$ and the reduction potentials of the copper complexes. Five such systems have been studied (Table II), and the average value calculated for the reduction potential of $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ is 0.813 V.

In these studies a value of 0.82 V was adopted as the formal reduction potential for the $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ couple, because the average value of $E°'$ from cyclic voltammetry was 0.83 V, while the average value from equilibrium or kinetic measurements was slightly greater than 0.81 V.

Kinetic Considerations. The redox reaction between the Ni(III,II) and Cu(III,II) deprotonated-peptide complexes is given in eq 3. For the majority of the Cu(III) complexes

$$Cu^{III}(H_{-n}L) + Ni^{II}(H_{-m}L')^- \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} Cu^{II}(H_{-n}L)^- + Ni^{III}(H_{-m}L') \quad (3)$$

$$Cu^{II}(H_{-n}L)^- \xrightarrow[\text{acid}]{k_D} Cu_{aq}^{2+} + HL \quad (4)$$

reaction 3 is thermodynamically unfavorable. However, in acidic media the $Cu^{II}(H_{-n}L)^-$ product readily dissociates to form aquocopper(II) and the protonated peptide ligand (eq 4). The rapid acid dissocation (eq 4) compensates for the thermodynamically unfavorable redox step (eq 3), making the overall reaction thermodynamically favorable.

With one exception, the reactions between Cu(II) and Ni(III) were thermodynamically favorable, which permitted the direct measurement of rate constants for the reverse of reaction 3 without the presence of an irreversible scavenging reaction. In the case of the thermodynamically unfavorable reaction between $Ni^{III}(H_{-2}G_2A)$ and $Cu^{II}(H_{-2}G_2A)^-$, the initial reactant concentrations were adjusted so that the reaction would go to at least 90% completion.

For the reactions in which the $Cu^{III}(H_{-n}L)$ complex was the limiting reagent (Table III), excellent pseudo-first-order plots of the absorbance–time data were obtained over at least 4 half-lives, which showed that the reactions were first order with respect to the $Cu^{III}(H_{-n}L)$ concentration. The observed rate constant, k_{obsd}, also exhibited a first-order dependence on the concentration of the $Ni^{II}(H_{-m}L')^-$ reductant (Figure 1). Thus, for the reactions of Cu(III) with excess Ni(II), the observed rate constant is related to the electron-transfer rate constant by eq 5.

$$k_{obsd} = k_{12}[Ni^{II}(H_{-m}L')^-] \quad (5)$$

When the $Ni^{III}(H_{-m}L')$ complex was the limiting reagent (Table IV), the absorbance–time data also exhibited pseudo-first-order dependence over at least 4 half-lives. The values of the pseudo-first-order rate constants depend on the concentration of the $Cu^{II}(H_{-n}L)^-$ reductant (Table IV) and are related to k_{21}, the electron-transfer rate constant for the reverse of reaction 3, by eq 6.

$$k_{obsd} = k_{21}[Cu^{II}(H_{-n}L)^-] \quad (6)$$

The buffer concentration and pH used for each set of reactions (Tables III and IV) were chosen to ensure that the following three criteria were met: (1) Only the fully deprotonated forms of the reactant complexes were present initially in appreciable concentrations. (2) The concentration of the $Cu^{II}(H_{-n}L)^-$ or $Ni^{II}(H_{-m}L')^-$ reducing agents did not change appreciably during the time of the observed redox reaction. (3) The electron-transfer reaction (eq 3) rather than the scavenging acid dissociation (eq 4) was rate determining.

Di- and trivalent nickel and copper deprotonated-peptide complexes can form outside-protonated species[20,22,32,33] in which a peptide oxygen is protonated, while all the metal–N(peptide) bonds remain intact (eq 7). The value of log K_{1H} for tripeptide

$$M(H_{-n}L) + H^+ \underset{}{\overset{K_{1H}}{\rightleftharpoons}} M(H_{-n}L)\cdot H^+ \quad (7)$$

and tripeptide amide complexes is approximately 2.[20,33] For tetrapeptide complexes such as $Ni^{II}(H_{-3}G_4)^{2-}$ and $Cu^{II}(H_{-3}G_4)^{2-}$, log K_{1H} is approximately 4.[22,32] To ensure that the fully deprotonated $M(H_{-n}L)$ species were the only effective reactants, the kinetics of each electron-transfer reaction was measured at a pH at least 1.5 units above the log K_{1H} values of the metal peptide complexes used. In addition, the pH independence of k_{obsd} was confirmed by varying the reaction pH (Tables III and IV).

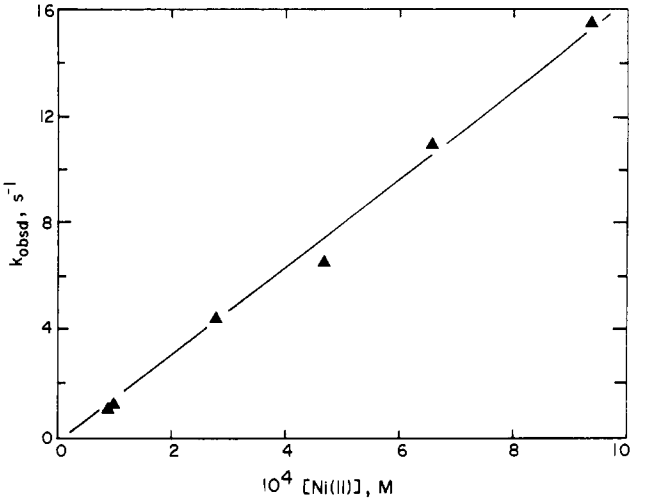

Figure 1. Variation in observed rate constant with Ni(II) concentration for the reaction of $Ni^{II}(H_{-3}G_4a)^-$ with $Cu^{III}(H_{-3}G_4a)$ (25.0 °C, μ = 0.5 ($NaClO_4$ + 0.25 M $HOAc_T$), slope 1.69 (±0.06) × 10^4 M^{-1} s^{-1}).

The Cu(III) deprotonated-peptide complexes are more stable in neutral solution because the intramolecular ligand oxidation decomposition is catalyzed by both acid and base.[32] In order to avoid interferences from these decomposition reactions, the kinetics of the Cu(III)–Ni(II) electron-transfer reactions were studied between pH 4 and 7. At these pH values the $Ni^{II}(H_{-m}L')$ complexes are unstable toward dissociation.[20,22] However, at pH 5 the pseudo-first-order rate constants of the redox reactions of $Ni^{II}(H_{-3}G_3a)^-$, $Ni^{II}(H_{-3}G_4a)^-$, and $Ni^{II}(H_{-2}Aib_3)^-$ with Cu(III) peptides (Table III) are at least 1 order of magnitude greater than the rate constants for Ni(II) acid dissociation reactions (Table V). Thus, when a solution of $Cu^{III}(H_{-n}L)$, buffered at pH 5, is mixed with an unbuffered (pH 10) solution of $Ni^{II}(H_{-m}L')^-$, the Cu(III)–Ni(II) electron-transfer reaction (eq 3) takes place before a significant amount of the Ni(II) complex can dissociate.

The kinetics of the $Cu^{II}(H_{-n}L)^-$ acid dissociation reactions (eq 4) have been investigated thoroughly for a wide variety of peptide ligands, L.[18,34,35] These reactions are catalyzed by general acids, HX, as well as by H_3O^+, and the dissociation rate constant k_D (eq 4) is given by eq 8.

$$k_D = k_{H_2O} + k_H[H^+] + k_{HX}[HX] \quad (8)$$

As was stated earlier, many oxidations of $Ni^{II}(H_{-m}L')^-$ complexes by $Cu^{III}(H_{-n}L)$ complexes (Table III) are thermodynamically unfavorable processes, driven to completion only because the initial $Cu^{II}(H_{-n}L)^-$ products (eq 3) are unstable with respect to dissociation (eq 4). Consequently,

(32) Rybka, J. S.; Kurtz, J. L.; Neubecker, T. A.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 2791.
(33) Raycheba, J. M. T.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 837.
(34) Bannister, C. E.; Margerum, D. W.; Raycheba, J. M. T.; Wong, L. F. *J. Chem. Soc., Faraday Trans. 1* **1975**, *10*, 78.
(35) Margerum, D. W.; Dukes, G. R. In "Metal Ions in Biological Systems"; Sigel, H., Ed.; Marcel Dekker: New York, 1974; Vol. 1, p 157.

Table III. Kinetic Data for the Oxidation of Some Nickel(II) Deprotonated-Peptide Complexes by a Series of Copper(III) Deprotonated-Peptide Complexes[a]

oxidant[b]	10^4[reductant], M	pH	k_{obsd},[c] s^{-1}	k_{12}, M^{-1} s^{-1}	oxidant[b]	10^4[reductant], M	pH	k_{obsd},[c] s^{-1}	k_{12}, M^{-1} s^{-1}
				Reductant = $Ni^{II}(H_{-3}G_4a)^-$					
$Cu^{III}(H_{-3}PG_2a)$	4.01	5.06	0.36 (1)	9.7×10^2	$Cu^{III}(H_{-3}G_4a)$	6.60	5.46	11.0 (3)	
	4.01	5.24	0.38 (1)			9.40	5.46	15.5 (3)	
	4.01	5.56	0.43 (1)			2.82	5.62	4.51 (7)	
$Cu^{III}(H_{-3}G_3Aa)$	11.5	4.86	1.62 (1)	1.40×10^3	$Cu^{III}(H_{-3}G_3AOCH_3)$	4.70	5.00	8.5 (7)	1.9×10^4
	11.5	5.18	1.59 (1)			4.70	5.43	8.7 (7)	
	11.5	5.46	1.62 (2)			4.70	5.66	9.3 (2)	
$Cu^{III}(H_{-3}VG_2a)$	11.5	4.80	1.24 (1)	1.08×10^3	$Cu^{III}(H_{-2}leu_3)$	2.00	5.03	43 (1)	2.1×10^5
	11.5	5.16	1.23 (1)			2.00	5.34	40 (1)	
	11.5	5.30	1.24 (1)			2.00	5.59	40 (1)	
$Cu^{III}(H_{-3}G_4)^-$	11.5	5.24	4.7 (1)	4.1×10^3	$Cu^{III}(H_{-3}G_5)^-$	15.4	4.68	12.4 (7)	8.6×10^3
	11.5	5.87	4.7 (1)				4.85	12.4 (9)	
$Cu^{III}(H_{-3}G_3a)$	11.5	5.05	4.42 (6)	3.83×10^3			5.12	12.4 (6)	
	11.5	5.38	4.39 (4)		$Cu^{III}(H_{-3}A_4)^-$	11.5	4.96	0.68 (2)	5.1×10^2
$Cu^{III}(H_{-3}G_4a)$	2.82	5.01	4.5 (2)	1.6×10^4			5.21	0.61 (3)	
	0.95	5.46	1.09 (5)				5.37	0.56 (3)	
	1.00	5.46	1.25 (6)		$Cu^{III}(H_{-3}A_5)^-$	11.5	4.92	0.34 (3)	2.9×10^2
	2.82	5.46	4.5 (1)				5.32	0.32 (1)	
	4.70	5.46	6.56 (3)						
				Reductant = $Ni^{II}(H_{-3}FG_2a)^-$					
$Cu^{III}(H_{-3}FG_2a)$	11.5	4.78	4.5 (3)	3.9×10^3	$Cu^{III}(H_{-3}G_4)^-$	11.5	5.18	4.8 (1)	4.1×10^3
		5.09	4.6 (2)				5.24	4.7 (1)	
		5.32	4.4 (2)				5.87	4.7 (1)	
				Reductant = $Ni^{II}(H_{-3}A_4)^{2-}$					
$Cu^{III}(H_{-3}A_5)^-$	11.5	4.81	2.55 (11)	2.1×10^2	$Cu^{III}(H_{-3}A_5)^-$		5.58	0.55 (2)	
		5.10	1.54 (14)				5.81	0.37 (1)	
		5.36	0.80 (7)						
				Reductant = $Ni^{II}(H_{-3}G_4a)^-$					
$Cu^{III}(H_{-2}A_3)$	2.11	5.00	47 (3)	2.3×10^5	$Cu^{III}(H_{-2}G_2A)$	1.00	5.43	56 (3)	
	2.11	5.42	48 (1)			1.00	5.65	62 (3)	
$Cu^{III}(H_{-2}GA_2)$	1.00	5.02	36 (2)	3.8×10^5	$Cu^{III}(H_{-2}G_3)$	2.30	5.00	267 (17)	1.2×10^6
	1.00	5.44	37 (2)		$Cu^{III}(H_{-2}G_2\beta A)$	1.00	5.01	127 (6)	1.4×10^6
	1.00	5.65	40 (1)			1.00	5.39	142 (9)	
$Cu^{III}(H_{-2}G_2A)$	1.00	5.02	61 (6)	6.0×10^5		1.00	5.64	146 (7)	
				Reductant = $Ni^{II}(H_{-2}Aib_3)^-$ [d]					
$Cu^{III}(H_{-3}PG_2a)$	3.89	3.99	0.262 (3)	6.7×10^2	$Cu^{III}(H_{-3}G_3AOCH_3)$	3.89	3.90	4.19 (8)	1.09×10^4
	3.89	4.39	0.259 (3)			3.89	4.36	4.32 (6)	
	3.89	4.87	0.263 (2)			3.89	4.85	4.16 (2)	
$Cu^{III}(H_{-3}G_3a)$	2.15	4.30	0.396 (6)	1.74×10^3	$Cu^{III}(H_{-2}leu_3)$	3.19	3.92	4.19 (8)	1.09×10^4
	4.30	4.30	0.777 (16)			3.19	4.33	4.32 (6)	
	8.60	4.30	1.45 (3)			3.19	4.82	4.16 (2)	
	12.9	4.30	2.21 (1)		$Cu^{III}(H_{-2}A_3)$	3.19	3.93	15.2 (1)	4.85×10^4
	3.75	4.04	0.65 (1)			3.19	4.33	15.5 (1)	
	3.75	4.17	0.65 (2)			3.19	4.82	15.7 (2)	
	3.75	4.59	0.67 (1)		$Cu^{III}(H_{-2}G_2A)$	2.79	3.92	69 (2)	2.46×10^5
	3.75	4.85	0.631 (5)			2.79	4.18	68 (2)	
	3.89	3.89	0.67 (1)			2.79	4.41	70 (2)	
	3.89	4.36	0.68 (1)		$Cu^{III}(H_{-2}G_2\beta A)$	2.79	3.92	147 (3)	5.29×10^5
	3.89	4.86	0.69 (1)			2.79	4.2	148 (16)	
$Cu^{III}(H_{-3}G_4a)$	3.89	3.97	2.38 (1)	6.25×10^3					
	3.89	4.36	2.45 (1)						
	3.89	4.86	2.46 (1)						
				Reductant = $Ni^{II}(H_{-3}G_3a)^-$					
$Cu^{III}(H_{-3}G_4)^-$	15.4	5.15	6.8 (3)	4.4×10^3	$Cu^{III}(H_{-3}G_5)^-$	15.4	4.68	12.7	8.2×10^3
	15.4	5.37	6.7 (3)			15.4	4.85	12.7	
						15.4	5.12	12.6	
				Reductant = $Ni^{II}(H_{-3}Aib_3a)^-$ [d]					
$Cu^{III}(H_{-2}leu_3)$	3.00	4.94	47.8 (9)	1.59×10^5	$Cu^{III}(H_{-2}A_3)$	3.00	5.05	61.5 (8)	2.05×10^5

[a] $T = 25.0$ °C, $\mu = 0.5$ (NaOAc + $NaClO_4$), $[HOAc]_T = 0.25$ M. [b] [oxidant] = (1–10) $\times 10^{-5}$ M, with [oxidant] ≤ [reductant]/10. [c] The standard deviation given in parentheses after the value of k_{obsd} is the uncertainty in the least significant digit(s). [d] $\mu = 0.1$ (NaOAc + $NaClO_4$), $[HOAc]_T = 0.05$ M.

the observed pseudo-first-order rate constant for the overall reaction (eq 3 and 4) is given by eq 9, where k_D is defined by

$$k_{obsd} = \frac{k_{12}k_D[Ni^{II}(H_{-m}L')^-]}{k_{21}[Ni^{III}(H_{-m}L')] + k_D} \quad (9)$$

eq 8 and $Cu^{II}(H_{-n}L)^-$ is assumed to be a steady-state species. If the observed reactions are limited by the electron-transfer step (eq 3), the condition that $k_D >> k_{21}[Ni^{III}(H_{-m}L')]$ must be fulfilled so that $k_{obsd} = k_{12}[Ni^{II}(H_{-m}L')^-]$.

The acid dissociation rate constants of several $Cu^{II}(H_{-n}L)^-$ complexes produced from reaction pairs listed in Table III have been measured.[17-19,36] In each case for which k_{H_2O}, k_H, and

(36) Wang, Y. H. C.; Margerum, D. W., to be submitted for publication.

Table IV. Kinetic Data for the Reduction of Several Nickel(III) Deprotonated-Peptide Complexes by a Series of Copper(II) Deprotonated-Peptide Complexes[a]

oxidant[b]	10^4[reductant], M	pH	k_{obsd},[c] s^{-1}	k_{21}, M^{-1} s^{-1}
	Reductant = $Cu^{II}(H_{-2}A_3)^-$			
$Ni^{III}(H_{-2}Aib_3)$	1.50	7.9	10.9 (5)	7.7×10^4
	2.00	8.1	17.1 (6)	
	4.00	8.1	33 (1)	
	8.00	8.0	65 (1)	
	12.0	8.1	94 (2)	
	16.0	8.1	123 (11)	
$Ni^{III}(H_{-3}Aib_3a)$	3.00	7.9	72 (2)	2.4×10^5
	Reductant = $Cu^{II}(H_{-2}G_2A)^-$ [d]			
$Ni^{III}(H_{-2}Aib_3)$	3.00	7.9	81 (5)	2.7×10^5
$Ni^{III}(H_{-2}G_2A)$	6.00	8.0	102 (5)	1.70×10^5
	Reductant = $Cu^{II}(H_{-2}leu_3)^-$			
$Ni^{III}(H_{-2}Aib_3)$	1.5	7.9	23.7 (3)	1.6×10^5
	Reductant = $Cu^{II}(H_{-3}G_3AOCH_3)^-$			
$Ni^{III}(H_{-2}Aib_3)$	1.5	7.9	88 (1)	5.9×10^5
	Reductant = $Cu^{II}(H_{-3}G_4a)^-$			
$Ni^{III}(H_{-2}Aib_3)$	1.5	7.9	200 (6)	1.3×10^6
	1.00	7.96	7.79 (16)	8.1×10^4
	1.60	7.91	12.8 (2)	
	2.00	7.95	16.3 (2)	
	3.00	7.95	24.9 (5)	
$Ni^{III}(H_{-3}Aib_3a)$	3.00	7.77	54 (2)	1.80×10^5
$Ni^{III}(H_{-3}G_3a)$	1.0	7.94	40 (1)	3.8×10^5
	1.6	7.90	66 (3)	
	2.0	7.91	78 (8)	
	3.0	7.89	116 (4)	
$Ni^{III}(H_{-3}G_4a)$	1.0	7.93	27.7 (6)	2.7×10^5
	1.6	7.88	43.6 (7)	
	2.0	7.88	55 (2)	
	3.0	7.82	81 (1)	
$Ni^{III}(H_{-2}A_3)$	1.38	8.0	25 (1)	1.8×10^5
$Ni^{III}(H_{-2}G_2A)$	3.0	7.90	81 (5)	2.7×10^5
	Reductant = $Cu^{II}(H_{-3}G_3a)^-$			
$Ni^{III}(H_{-2}Aib_3)$	1.5	8.10	241 (7)	1.6×10^6
	Reductant = $Cu^{II}(H_{-3}Aib_3a)^-$ [d]			
$Ni^{III}(H_{-2}Aib_3)$	2.0	8.0		2.2×10^6 [e]

[a] $T = 25.0$ °C, $\mu = 0.1$ ($Na_2B_4O_7$ + $NaClO_4$), [borate] = 0.002 M. [b] [oxidant] = $(1\text{-}10) \times 10^{-5}$ M, with [oxidant] ≤ [reductant]/10. [c] The standard deviations in the least significant digit(s) are given in parentheses. [d] $\mu = 0.1$ (NaH_2PO_4 + Na_2HPO_4), $[H_3PO_4]_T$ = 0.05 M. [e] Extrapolated value from lower temperatures.

Table V. Acid Dissociation Rate Constants for Ni(II) Peptide Reductants

Ni(II) peptide	pH	k_{obsd}, s^{-1}	Ni(II) peptide	pH	k_{obsd}, s^{-1}
$Ni^{II}(H_{-3}G_3a)^-$	4.9	0.56[a]	$Ni^{II}(H_{-2}Aib_3)^-$	4.1	0.002[c]
$Ni^{II}(H_{-3}G_4a)^-$	5.1	0.022[b]			

[a] Reference 22, 25.0 °C, $\mu = 0.1$ ($NaClO_4$ + NaOAc). [b] Reference 20. [c] This work, 25.0 °C, $\mu = 0.1$ ($NaClO_4$ + NaOAc).

k_{HX} are known or can be estimated,[36] the calculated value of $k_D/k_{21}[Ni^{III}(H_{-m}L')]$ is greater than or equal to 90 at pH ≲5.5. Therefore, $k_{obsd} = k_{12}[Ni^{II}(H_{-m}L')^-]$, and the electron-transfer step is rate determining.

The mechanism shown in eq 3 and 4 can be verified by examining the dependence of reaction 3 on the concentration of $Ni^{III}(H_{-m}L')$ at a pH where $k_D \geq k_{21}[Ni^{III}(H_{-m}L')]$ or by measuring k_{21} directly and calculating the equilibrium constant or cell potential for eq 3 from the kinetic data. At pH 3, the half-life for the intramolecular redox decomposition of $Ni^{III}(H_{-3}G_3a)$ is ~15 min and the half-life of $Ni^{III}(H_{-3}G_4a)$ is only slightly longer.[3] Thus, the use of $Ni^{III}(H_{-3}G_3a)$ or $Ni^{III}(H_{-3}G_4a)$ for either of the above tests is difficult. However, the exceptional thermal stability of $Ni^{III}(H_{-2}Aib_3)$ greatly facilitates these tests.[5] The dependence of the observed rate

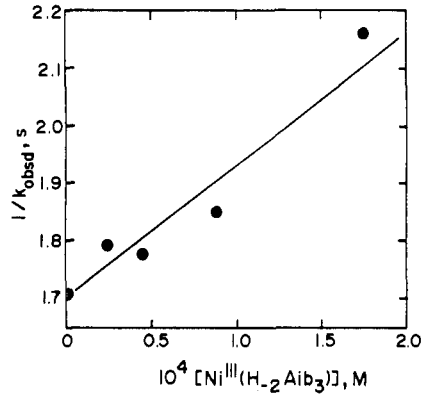

Figure 2. Dependence of the reciprocal of the observed rate constant for the reaction of $Cu^{III}(H_{-3}G_3a)$ with $Ni^{II}(H_{-2}Aib_3)^-$ on the $Ni^{III}(H_{-2}Aib_3)$ concentration that shows the inhibition of the overall reaction by Ni(III) ($[Ni^{II}(H_{-2}Aib_3)^-]_0 = 3.38 \times 10^{-4}$ M, 25.0 °C, $\mu = 0.1$ ($NaClO_4$ + 0.05 M $HOAc_T$)).

constant for the reaction between $Cu^{III}(H_{-3}G_3a)$ and $Ni^{II}(H_{-2}Aib_3)^-$ at pH 5.6 on the concentration of $Ni^{III}(H_{-2}Aib_3)$ is shown in Figure 2. The observed linear relationship between $1/k_{obsd}$ and $[Ni^{III}(H_{-2}Aib_3)]$ would be expected only if eq 9 were valid. The slope of the least-squares line in Figure 2 is $(2.5 \pm 0.3) \times 10^3$ M^{-1} s, and under the reaction conditions k_D for $Cu^{II}(H_{-3}G_3a)^-$ is estimated to be 1.3×10^3 s^{-1}.[36] With this information and $[Ni^{II}(H_{-2}Aib_3)^-] = 3.38 \times 10^{-4}$ M, the cell potential for the reaction $Cu^{III}(H_{-3}G_3a) + Ni^{II}(H_{-2}Aib_3)^- \rightleftarrows Cu^{II}(H_{-3}G_3a)^- + Ni^{III}(H_{-2}Aib_3)$ is calculated to be −0.18 V, in excellent agreement with the electrochemically determined value (Table I). Thus, the $Ni^{III}(H_{-2}Aib_3)$ inhibition data confirm the validity of the reaction sequence given in eq 3 and 4.

A final confirmation that the electron-transfer reaction (eq 3) is rate determining can be obtained by calculating the cell potential from kinetic data for those reactions that were run in both the forward (Table III) and reverse (Table IV) directions. The cell potentials, $\Delta E^{\circ\prime}$, for several reactions of Cu(III,II) peptides with $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ are given in Table II. In each case the reduction potential for $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ obtained as the sum of the cell potential and the reduction potential of the Cu(III,II) complex is close to the value obtained by cyclic voltammetry.

Inner-Sphere vs. Outer-Sphere Mechanisms. The electron-transfer reactions between Cu(II) peptides and Cu(III) peptides occur by an outer-sphere mechanism.[14] A number of observations indicate that for the nickel(III,II) peptides inner-sphere mechanisms may be more important than for copper(III,II) peptides.

Cross-reactions between Ni(III) and Ni(II) peptides are catalyzed by millimolar concentrations of bromide, chloride, or azide ions.[15] On the other hand chloride ion, even at 1 M concentrations, does not affect the rate of the $Cu^{III,II}(H_{-2}Aib_3)^{0,-}$ self-exchange reactions.[13] The electron-transfer rates between $Ni^{III}(H_{-2}Aib_3)$ and $Cu^{II}(H_{-2}Aib_3)^-$ are not affected by bromide ion, even at 0.4 M concentration. Similarly, no bromide ion effect is observed for the reaction between $Ni^{III}(H_{-2}Aib_3)$ and $Cu^{II}(H_{-2}A_3)^-$.

It appears that in Ni(III)–Ni(II) reactions, where the electron moves from a reductant to an oxidant d_{z^2} orbital, halide ions can serve as effective axial-briding ligands for an inner-sphere pathway. In Cu(III)–Cu(II) reactions, where the electron is transferred from one $d_{x^2-y^2}$ orbital to another, axial bridging is less effective in enhancing the reaction rate. Bromide ion does not facilitate inner-sphere electron transfer from Cu(II) to Ni(III).

Additional support for the proposition that inner-sphere mechanisms are more important in Ni(III)–Ni(II) than in

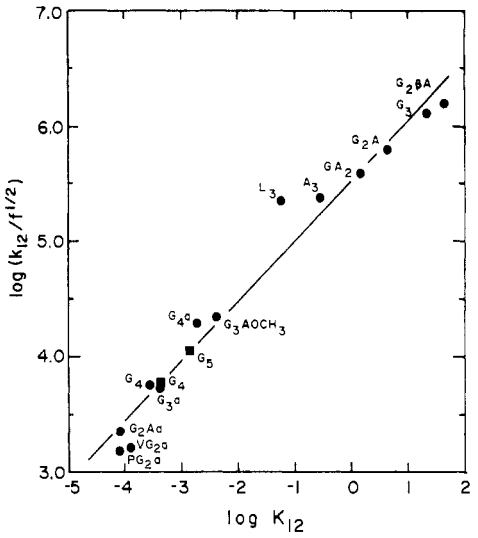

Figure 3. Marcus free energy correlation for the oxidation of $Ni^{II}(H_{-3}G_3a)^-$ (■) and $Ni^{II}(H_{-3}G_4a)^-$ (●) by a series of Cu(III) peptides.

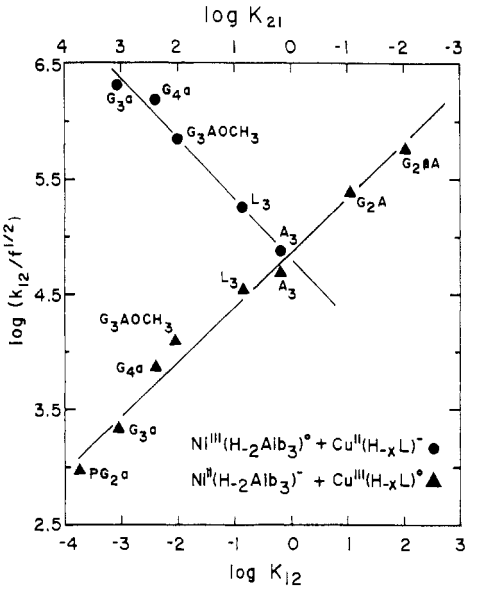

Figure 4. Marcus free energy correlations for the redox reactions of $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ with a series of $Cu^{III,II}(H_{-n}L)^{0,-}$ complexes: Ni(III) + Cu(II) (●); Ni(II) + Cu(III) (▲). $K_{12} = [Ni^{III}][Cu^{II}]/[Cu^{III}][Ni^{II}]$; $K_{21} = 1/K_{12}$.

Cu(III)–Cu(II) reactions comes from two observations. (1) In the oxidation of the divalent metal complex by $IrCl_6^{2-}$, the k_{obsd}/k_{OS} ratio (where k_{OS} is the calculated outer-sphere electron-transfer rate constant) is at least 1 order of magnitude larger for Ni(II) than for Cu(II).[37] (2) In the reduction of the trivalent metal complex by iodide ion, the formation constant for the axially bonded M^{III}–I^--activated complex is larger for Ni^{III} than for Cu^{III}.[38]

Reactions of Ni(III) peptides with reducing agents such as $Ru(NH_3)_5py^{2+}$, where the electron transfer must proceed by an outer-sphere mechanism, are much slower[16] than expected from the calculated self-exchange rate constants obtained from Ni(III) peptide–Ni(II) peptide reactions.[15] This suggests that the latter reactions follow an inner-sphere or enhanced pathway for electron transfer.

Marcus Correlations. In terms of Marcus' theory of electron transfer,[39-41] the rate constants, k_{12} or k_{21}, for exchange cross-reactions such as those between Cu(III,II) and Ni(III,II) peptide complexes (eq 1) can be related to the self-exchange rate constants, k_{11} and k_{22} (eq 10 and 11), by eq 12 and 13, where K_{12} or K_{21} is the equilibrium constant for the cross-reaction and Z, the bimolecular collision frequency, is taken as 10^{11} M^{-1} s^{-1}. The equilibrium constants are calculated from the potentials given in Table I.

$$Ni^{III}(H_{-m}L') + Ni^{*II}(H_{-m}L')^- \underset{}{\overset{k_{11}}{\rightleftharpoons}} Ni^{*III}(H_{-m}L') + Ni^{II}(H_{-m}L')^- \quad (10)$$

$$Cu^{III}(H_{-n}L) + Cu^{*II}(H_{-n}L)^- \overset{k_{22}}{\rightleftharpoons} Cu^{*III}(H_{-n}L) + Cu^{II}(H_{-n}L)^- \quad (11)$$

$$k_{12} = (k_{11}k_{22}K_{12}f)^{1/2} \quad (12)$$

$$\log f = (\log K)^2/[4 \log (k_{11}k_{22}/Z^2)] \quad (13)$$

Equation 12 predicts that log $(k_{12}/f^{1/2})$ will be linearly related to log K_{12} for cross-reactions in which the self-exchange rate constants for a series of redox couples are the same. The Cu(III,II) peptide complexes come close to meeting this criterion. Although the Cu(III,II) reduction potential is very dependent on the nature of the peptide ligand, the range of the values of the Cu(III,II) self-exchange rate constants, k_{22}, is small.[13,14] If these reactions are outer sphere, it should be possible to determine the self-exchange rate constant, k_{11}, for a given nickel peptide complex from the measured rate constants, k_{12} or k_{21}, for the reaction of the $Ni(H_{-m}L')$ complex with a series of copper peptides.

A plot of log $(k/f^{1/2})$ vs. log K for reactions of $Ni^{II}(H_{-3}G_4a)^-$ and $Ni^{II}(H_{-3}G_3a)^-$ with a series of Cu(III) peptides is shown in Figure 3. For the reactions in which $Ni^{II}(H_{-3}G_4a)^-$ is the reductant (Table III), the least-squares slope and intercept are 0.52 (±0.03) and 5.50 (±0.08), respectively. The data for the $Ni^{II}(H_{-3}G_3a)^-$ reactions fall on this same correlation line. With use of a value of $k_{22} = 5.5 \times 10^4$ M^{-1} s^{-1} for the doubly deprotonated copper peptide complexes[13] and of $k_{22} = 2 \times 10^4$ M^{-1} s^{-1} for the triply deprotonated complexes,[14] the apparent self-exchange rate constant, k_{11}, for both $Ni^{III,II}(H_{-3}G_4a)^{0,-}$ and $Ni^{III,II}(H_{-3}G_3a)^{0,-}$ is 1.8×10^6 M^{-1} s^{-1}.

For the reactions of Cu(III) peptides with $Ni^{II}(H_{-2}Aib_3)^-$, the plot of log $(k/f^{1/2})$ vs. log K (Figure 4) has a slope of 0.47 (±0.02) and an intercept of 4.84 (±0.05). For the reverse reaction, $Ni^{III}(H_{-2}Aib_3)$ with Cu(II) peptides, the slope and intercept are 0.46 (±0.05) and 4.84 (±0.09), respectively. A value of 8.7×10^4 M^{-1} s^{-1} is obtained for the apparent self-exchange rate constant of $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$, regardless of the direction of the Cu–Ni reactions.

The reactions of $Cu^{II}(H_{-2}Aib_3)^-$ and $Cu^{II}(H_{-3}Aib_3a)^-$ with $Ni^{III}(H_{-2}Aib_3)$ are omitted from Figure 4 because they do not fall on the correlation line. The behavior of the Aib_3 complexes differs significantly from that of other peptide complexes. Although the self-exchange rate constants for the Cu(III,II) peptides (k_{22}) are approximately the same for different peptides with values[13,14] between 2×10^4 and 5.5×10^4 M^{-1} s^{-1}, this is not the case with the Ni(III,II) reactions.

Self-exchange rate constants for Ni(III,II) peptide complexes have been calculated recently from the measured rate constants for a series of Ni(III)–Ni(II) cross-reactions.[15] These values, which depend strongly on the nature of the peptide ligand, are 1.2×10^5 M^{-1} s^{-1} for triply deprotonated peptides, 1.3×10^4 M^{-1} s^{-1} for doubly deprotonated peptides other than Aib_3, and 5.5×10^2 M^{-1} s^{-1} for $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$. The Ni(III,II) self-exchange rate constants obtained from copper–nickel reactions are not the same. When the copper peptide ligand is Aib_3 or Aib_3a, the values are smaller than

(37) Owens, G. W.; Margerum, D. W. *Anal. Chem.* **1980**, *52*, 91A.
(38) Raycheba, J. M. T.; Margerum, D. W. *Inorg. Chem.* **1981**, *20*, 1441.
(39) Marcus, R. A. *J. Chem. Phys.* **1956**, *24*, 966.
(40) Marcus, R. A. *Discuss. Faraday Soc.* **1960**, *29*, 21.
(41) Marcus, R. A. *J. Phys. Chem.* **1963**, *67*, 853, 2889.

Table VI. Comparison of the Observed and Calculated Second-Order Rate Constants for the Nickel(III,II) and Copper(III,II) Deprotonated-Peptide Complex Redox Reactions[a]

oxidant	reductant	ΔE, V	f[b]	log k_{12} or log k_{21} obsd	log k_{12} or log k_{21} calcd[c]
$Cu^{III}(H_{-3}PG_2a)$[d]	$Ni^{II}(H_{-2}Aib_3)^-$[f]	−0.22	0.58	2.83	1.54
$Cu^{III}(H_{-3}G_3a)$[d]		−0.18	0.69	3.24	1.92
$Cu^{III}(H_{-3}G_4a)$[d]		−0.14	0.80	3.80	2.29
$Cu^{III}(H_{-3}G_3AOCH_3)$[d]		−0.12	0.85	4.04	2.47
$Cu^{III}(H_{-2}leu_3)$[e]		−0.05	0.95	4.53	3.31
$Cu^{III}(H_{-2}A_3)$[e]		−0.01	1.00	4.69	3.66
$Cu^{III}(H_{-2}G_2A)$[e]		0.06	0.96	5.39	4.24
$Cu^{III}(H_{-2}G_2\beta A)$[e]		0.12	0.85	5.72	4.72
$Ni^{III}(H_{-2}Aib_3)$[f]	$Cu^{II}(H_{-2}A_3)^-$[e]	0.01	1.00	4.86	3.82
	$Cu^{II}(H_{-2}leu_3)^-$[e]	0.05	0.97	5.20	4.16
	$Cu^{II}(H_{-3}G_3AOCH_3)^-$[d]	0.12	0.85	5.77	4.50
	$Cu^{II}(H_{-3}G_4a)^-$[d]	0.14	0.80	6.11	4.66
	$Cu^{II}(H_{-3}G_3a)^-$[d]	0.18	0.69	6.20	4.96
$Ni^{III}(H_{-2}G_2A)$[g]	$Cu^{II}(H_{-2}G_2A)^-$[e]	−0.03	0.99	5.16	4.17
$Cu^{III}(H_{-2}G_2A)$[e]	$Ni^{II}(H_{-2}G_2A)^-$[g]	0.03	0.99	5.74	4.68
$Cu^{III}(H_{-3}PG_2a)$[d]	$Ni^{II}(H_{-3}G_4a)^-$[h]	−0.24	0.46	2.99	2.49
$Cu^{III}(H_{-3}G_2Aa)$[d]		−0.24	0.46	3.15	2.49
$Cu^{III}(H_{-3}VG_2a)$[d]		−0.23	0.49	3.03	2.59
$Cu^{III}(H_{-3}G_4)^-$[d]		−0.21	0.55	3.61	2.79
$Cu^{III}(H_{-3}G_3a)$[d]		−0.20	0.58	3.58	2.88
$Cu^{III}(H_{-3}G_5)^-$[d]		−0.18	0.66	3.88	3.09
$Cu^{III}(H_{-3}G_4a)$[d]		−0.16	0.71	4.20	3.26
$Cu^{III}(H_{-3}G_3AOCH_3)$[d]	$Ni^{II}(H_{-3}G_4a)^-$[h]	−0.14	0.77	4.28	3.45
$Cu^{III}(H_{-2}leu_3)$[e]		−0.07	0.94	5.32	4.30
$Cu^{III}(H_{-2}A_3)$[e]		−0.03	0.99	5.36	4.65
$Cu^{III}(H_{-2}GA_2)$[e]		0.01	1.00	5.58	4.99
$Cu^{III}(H_{-2}G_2A)$[e]		0.04	0.98	5.78	5.24
$Cu^{III}(H_{-2}G_3)$[e]		0.08	0.92	6.08	5.57
$Cu^{III}(H_{-2}G_2\beta A)$[e]		0.10	0.87	6.14	5.72
$Cu^{III}(H_{-3}G_4)^-$[d]	$Ni^{II}(H_{-3}G_3a)^-$[h]	−0.20	0.58	3.64	2.88
$Cu^{III}(H_{-3}G_5)^-$[d]		−0.17	0.68	3.91	3.17
$Cu^{III}(H_{-2}leu_3)$[e]	$Ni^{II}(H_{-3}Aib_3a)^-$[h]	−0.045	0.97	5.11	4.52
$Cu^{III}(H_{-2}A_3)$[e]		−0.005	1.00	5.31	4.87
$Cu^{III}(H_{-3}PG_2a)$[d]	$Ni^{II}(H_{-3}PG_2a)^-$[h]	−0.21	0.56	3.59	2.80
$Cu^{III}(H_{-3}G_4)^-$[d]		−0.20	0.59	3.62	2.90
$Cu^{III}(H_{-3}A_4)^-$[d]	$Ni^{II}(H_{-3}G_4a)^-$[h]	−0.24	0.47	2.71	2.51
$Cu^{III}(H_{-3}A_5)^-$[d]		−0.26	0.41	2.46	2.81
$Cu^{III}(H_{-3}A_5)^-$[d]	$Ni^{II}(H_{-3}A_4)^{2-}$[h]	−0.24	0.47	2.32	2.51
$Ni^{III}(H_{-2}Aib_3)$[f]	$Cu^{II}(H_{-2}Aib_3)^-$[e]	0.16	0.75	4.91	5.03
$Ni^{III}(H_{-2}Aib_3)$[f]	$Cu^{II}(H_{-3}Aib_3a)^-$[d]	0.45	0.11	6.34	6.84
$Ni^{III}(H_{-3}Aib_3a)$[h]	$Cu^{II}(H_{-2}Aib_3)^-$[e]	0.155	0.75	5.26	6.15
$Ni^{III}(H_{-3}G_3a)$[h]		0.17	0.68	5.58	6.26
$Ni^{III}(H_{-3}G_4a)$[h]		0.18	0.65	5.43	6.34
$Ni^{III}(H_{-2}A_3)$[g]		0.18	0.67	5.26	5.86
$Ni^{III}(H_{-2}G_2A)$[g]		0.19	0.64	5.43	5.94

[a] $T = 25.0$ °C, $\mu = 0.10$ ($NaClO_4$). [b] Calculated by using eq 13 and the indicated values of k_{11} and k_{22}. [c] Calculated by using eq 12 and the indicated values of k_{11} and k_{22}. [d] $k_{22} = 2 \times 10^4$ M^{-1} s^{-1}. [e] $k_{22} = 5.5 \times 10^4$ M^{-1} s^{-1}. [f] $k_{11} = 5.5 \times 10^2$ M^{-1} s^{-1}. [g] $k_{11} = 1.3 \times 10^4$ M^{-1} s^{-1}. [h] $k_{11} = 1.2 \times 10^5$ M^{-1} s^{-1}.

Table VII. Influence of Peptide Ligands on the Rates of Cu(III,II)-Ni(III,II) Electron-Transfer Reactions[a]

reactants		no. of systems	proposed mechanism			log k_{12}^{obsd} − log k_{12}^{calcd}
Cu complex	Ni complex		Cu(III)–Cu(II)	Ni(III)–Ni(II)	Cu–Ni	
1. $Cu^{III,II}(H_{-n}L)^{0,-}$[b]	$Ni^{III,II}(H_{-2}Aib_3)^{0,-}$	13	OS[d]	H[e]	E	1.24 ± 0.19
2. $Cu^{III,II}(H_{-2}L)^{0,-}$[c]	$Ni^{III,II}(H_{-2}L')^{0,-}$[c]	2	OS	E[f]	E	1.02 ± 0.05
3. $Cu^{III}(H_{-n}L)^b$	$Ni^{II}(H_{-3}L')^-$	20	OS	E	E	0.68 ± 0.18
4. $Cu^{III}(H_{-3}A_5)^-$	$Ni^{II}(H_{-3}L')$	3	OS	E	H	−0.11 ± 0.28
5a. $Cu^{II}(H_{-2}Aib_3)^-$	$Ni^{III}(H_{-2}Aib_3)$	1	OS	H	H	−0.12
5b. $Cu^{II}(H_{-3}Aib_3a)^-$	$Ni^{III}(H_{-2}Aib_3)$	1	OS	H	H	−0.50
6. $Cu^{II}(H_{-2}Aib_3)^-$	$Ni^{III}(H_{-m}L')^c$	5	OS	E	H	−0.71 ± 0.15

[a] $T = 25.0$ °C. [b] Excluding the Aib_3 and Aib_3a complexes. [c] Excluding the Aib_3 complex. [d] Outer sphere. [e] H = Hindered. [f] E = Enhanced.

those obtained from Ni(III)–Ni(II) cross-reactions; otherwise they are larger.

These discrepancies led us to examine the relationship between the nature of the peptide ligands and the differences between the observed and calculated second-order rate constants for a series of copper–nickel electron-transfer reactions (Table VI). The results of these calculations, based on the k_{11} values obtained from Ni(III,II) peptide cross-reactions, are plotted in Figure 5.

When the values of (log k_{12}^{obsd} − log k_{12}^{calcd}) are placed in groups corresponding to reactions of $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$, other doubly deprotonated nickel peptides, and triply deprotonated nickel peptides (Table VII), some patterns begin to emerge. With the exception of reactions involving $Cu^{II}(H_{-2}Aib_3)^-$ or

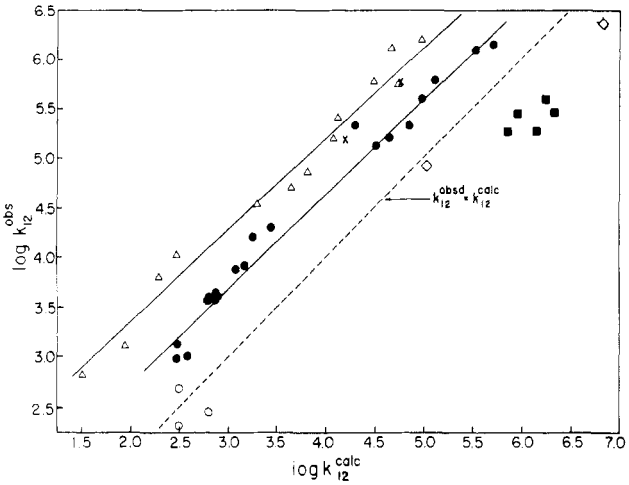

Figure 5. Plot of log k_{12}^{obsd} against log k_{12}^{calcd} for the reactions of $Cu^{III,II}(H_{-n}L)^{0,-}$ with $Ni^{III,II}(H_{-m}L')$. Reactant pairs (as given in Table VII): △ = set 1; × = set 2; ● = set 3; ○ = set 4; ◇ = set 5; ■ = set 6.

$Cu^{II}(H_{-3}Aib_3a)^-$, k_{12}^{obsd} is significantly larger than k_{12}^{calcd}, with the difference being greatest for reactions of $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ and least for reactions of triply deprotonated nickel complexes. For the reaction of $Cu^{II}(H_{-2}Aib_3)^-$ with $Ni^{III}(H_{-2}Aib_3)$, there is little difference between k_{12}^{obsd} and k_{12}^{calcd}, but for other reactions of $Cu^{II}(H_{-2}Aib_3)^-$, k_{12}^{obsd} is significantly smaller than k_{12}^{calcd}.

To account for these results we propose the following explanation. As discussed earlier, reactions between copper(II) and copper(III) complexes probably proceed exclusively by an outer-sphere mechanism (designated OS in Table VII). In contrast, reactions between nickel(II) and nickel(III) peptides appear to proceed by an inner-sphere or enhanced (E) mechanism. However, reactions of $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ complexes are sterically hindered (H) because the methyl groups of the Aib_3 ligand prevent close approach of the oxidant and reductant molecules.[15] For a given system the rate constants for the E mechanisms are greater than those for the H mechanisms, which in turn are larger than those for the OS mechanisms. For the copper–nickel reactions that proceed by an E mechanism (first three rows in Table VII) k_{obsd} is greater than k_{calcd} because the copper participates in an enhanced rather than an outer-sphere mechanism. The fact that the effect is greatest for reactions involving $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ suggests that this complex is less hindered in its reactions with copper than in its reactions with nickel peptides.

Reactions of nickel peptides with $Cu^{II}(H_{-2}Aib_3)^-$ and $Cu^{II}(H_{-3}Aib_3a)^-$, where k_{12}^{obsd} is less than k_{12}^{calcd}, (last three rows of Table VII) appear to be sterically hindered by the presence of the methyl groups on the Aib_3 ligands. The effect is smallest for reactions with $Ni^{III}(H_{-2}Aib_3)$, where the value of the Ni(III,II) self-exchange constant is already diminished by steric hindrance.

Two mechanisms that account for the differences between k_{12}^{obsd} and k_{12}^{calcd} suggest themselves. The electron transfer might proceed through a water bridge between the copper and nickel atoms. Alternatively, the nickel d_{z^2} orbital might interact with a coordinated copper peptide nitrogen, thereby bringing the nickel d_{z^2} and copper $d_{x^2-y^2}$ orbitals into close proximity and facilitating electron transfer from one metal to the other. The latter mechanism accounts for the fact that the log k_{12}^{obsd} – log k_{12}^{calcd} values are more sensitive to the nature of the copper peptide than to that of the nickel peptide. It also accounts for the anomalously low values of k_{12}^{obsd} in the reactions of $Cu^{III}(H_{-3}A_4)^-$ and $Cu^{III}(H_{-3}A_5)^-$ (Table VII, Figure 5). In these cases one side of the complex is blocked by the methyl groups on the first three alanyl residues, while the fourth and fifth alanyl residues block the other side. Thus, as in the case of $Cu^{II}(H_{-2}Aib_3)^-$, the close approach of a nickel d_{z^2} orbital necessary for bridging or interaction with a coordinated peptide nitrogen is sterically hindered.

Conclusions

Nickel(III,II) deprotonated-peptide complexes undergo rapid electron-transfer reactions with copper(III,II) peptides. The presence of bromide ion does not increase the rates of these reactions, in contrast to the large acceleration caused by bromide ion in the Ni(III)–Ni(II) cross-reactions.

The linear free energy dependences exhibited by various groups of copper–nickel cross-reactions are each consistent with those predicted by the Marcus theory. However, calculations of apparent self-exchange rate constants for Ni(III,II) peptides from these reactions give values that depend upon the type of coordinated peptide. These k_{11} values also differ from the values obtained from Ni(III)–Ni(II) cross-reactions.

The Marcus theory is rigorous for outer-sphere electron transfer, but it appears that none of the nickel–nickel or copper–nickel electron-transfer reactions are actually outer-sphere processes. When reactants are chosen that force an outer-sphere pathway for nickel(III,II) reactions[16] the self-exchange rate constants are many orders of magnitude lower than those obtained from the nickel(III) peptide–nickel(II) peptide cross-reactions.[15] Nevertheless, Marcus correlations hold for weak inner sphere interactions as observed[42,43] in the reactions of Cu(III) peptides with $IrCl_6^{3-}$ and with $Fe(CN)_6^{4-}$.

Differences between the observed and calculated second-order rate constants for reactions between copper and nickel peptides may be explained in terms of the pathway of electron transfer. Except for those cases where a bulky ligand prevents close approach of the oxidant and reductant species, there appears to be a directional enhancement by axial interaction of nickel with the copper complex. Thus, in Table VII the observed cross-reaction rate constants for $Cu^{III,II}(H_{-n}L)^{0,-}$ with $Ni^{III,II}(H_{-2}Aib_3)^{0,-}$ are a factor of 17 larger than the calculated rate constants. We believe that this is because the exchange cross-reaction is enhanced, while the copper self-exchange reactions are outer-sphere and the nickel self-exchange reactions are sterically hindered inner sphere.

Steric hindrance of the cross reaction is greater when the bulky ligand is attached to copper than when it is coordinated to nickel. Thus, the observed rates of reaction of $Cu^{II}(H_{-2}Aib_3)^-$ with $Ni^{III}(H_{-m}L')$ are a factor of 5 slower than calculated. In the reaction of $Cu^{II}(H_{-2}Aib_3)^-$ with $Ni^{III}(H_{-2}Aib_3)$ the values of k_{12}^{obsd} and k_{12}^{calcd} are nearly identical because both the Ni(III,II) self-exchange reaction and the Cu–Ni cross-reaction are sterically hindered.

The differences between k_{12}^{obsd} and k_{12}^{calcd} for these reactions are small, but they follow a consistent pattern that we believe it would be inappropriate to ignore. Obviously, more work is needed to establish the nature of the interactions.

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Registry No. $Cu^{III}(H_{-3}PG_2a)$, 24212-63-3; $Cu^{III}(H_{-3}G_3Aa)$, 89462-02-2; $Cu^{III}(H_{-3}VG_2a)$, 62801-40-5; $Cu^{III}(H_{-3}G_4)^-$, 57692-61-2; $Cu^{III}(H_{-3}G_3a)$, 62801-36-9; $Cu^{III}(H_{-3}G_4a)$, 68550-44-7; $Cu^{III}(H_{-3}G_3AOCH_3)$, 69042-73-5; $Cu^{III}(H_{-2}leu_3)$, 69042-72-4; $Cu^{III}(H_{-3}G_5)^-$, 68550-43-6; $Cu^{III}(H_{-3}A_4)^-$, 68628-66-0; $Cu^{III}(H_{-3}A_5)^-$, 62882-63-7; $Cu^{III}(H_{-3}FG_2a)$, 68550-42-5; $Cu^{III}(H_{-2}A_3)$, 69042-71-3; $Cu^{III}(H_{-2}GA_2)$, 69814-92-2; $Cu^{III}(H_{-2}G_2A)$, 69814-93-3; $Cu^{III}(H_{-2}G_3)$, 69814-94-4; $Cu^{III}(H_{-2}G_2\beta A)$, 69814-95-5; $Cu^{III}(H_{-3}G_2Aa)$, 62801-

(42) Owens, G. D.; Margerum, D. W. *Inorg. Chem.* **1981**, *20*, 1446.
(43) Anast, J. M.; Margerum, D. W. *Inorg. Chem.* **1982**, *21*, 3494.

38-1; $Cu^{II}(H_{-2}A_3)^-$, 42179-70-4; $Cu^{II}(H_{-2}leu_3)^-$, 29575-61-9; $Cu^{II}(H_{-3}G_3AOCH_3)^-$, 62882-66-0; $Cu^{II}(H_{-3}G_4a)^-$, 62801-43-8; $Cu^{II}(H_{-3}G_3a)^-$, 62801-35-8; $Cu^{II}(H_{-2}G_2A)^-$, 36515-85-2; $Cu^{II}(H_{-2}Aib_3)^-$, 89438-84-6; $Cu^{II}(H_{-3}Aib_3a)^-$, 85926-43-8; $Ni^{II}(H_{-2}Aib_3)^-$, 76757-48-7; $Ni^{II}(H_{-3}G_4a)^-$, 34722-99-1; $Ni^{II}(H_{-3}FG_2a)^-$, 89438-85-7; $Ni^{II}(H_{-3}A_4)^{2-}$, 62006-66-0; $Ni^{II}(H_{-3}G_4a)^-$, 34722-99-1; $Ni^{II}(H_{-3}G_3a)^-$, 34722-97-9; $Ni^{II}(H_{-3}Aib_3a)^-$, 89438-86-8; $Ni^{II}(H_{-2}G_2A)^-$, 19330-49-5; $Ni^{III}(H_{-2}Aib_3)$, 69990-32-5; $Ni^{III}(H_{-3}Aib_3a)$, 89438-87-9; $Ni^{III}(H_{-2}G_2A)$, 89438-88-0; $Ni^{III}(H_{-3}G_3a)$, 60165-87-9; $Ni^{III}(H_{-3}G_4a)$, 60108-87-4; $Ni^{III}(H_{-2}A_3)$, 62006-71-7.

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Complexes of $TiCl_4$ of Interest in Friedel–Crafts Reactions

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Nuclear magnetic resonance studies of systems with $TiCl_4$ and HCl and dimethyl ether, acetyl chloride, acetophenone, or methyl mesityl ketone have provided positive identification of the various complexes that exist in these systems. The ternary complex of ketone, HCl, and $TiCl_4$ is shown to be the product first formed in the $TiCl_4$-mediated Friedel–Crafts reaction of acetyl chloride and mesitylene. The relatively slow Friedel–Crafts reaction in this system is due to charge-transfer complex formation between $TiCl_4$ and the aromatic.

Introduction

Complex formation between $TiCl_4$ and dimethyl ether to give a 1:1 complex has been briefly reported.[2] Both 1:1 and 1:2 complexes of $TiCl_4$ with acetophenone have been described.[3-5] Only a 1:1 complex has been reported with acetyl chloride.[6-9]

Since all these studies involved neat reactants it seemed worthwhile to investigate these systems in a dilute solution with an inert solvent. Sulfur dioxide shows a slight tendency to complex with $TiCl_4$ since a 1:1 complex separates at high $TiCl_4$ concentration.[10] It has been found that both $AlCl_3$ and $SnCl_4$ form ternary complexes with HCl and an oxygen donor such as dimethyl ether or acetophenone.[11] Therefore, it was decided to study all these systems under comparable conditions in sulfur dioxide as solvent.

Experimental Section

^1H and ^{13}C resonance spectra were obtained on a Varian Associates XL-100 spectrometer equipped with a Nicolet Fourier transform attachment. All spectra are reported with respect to tetramethylsilane, although neopentane was used as an internal reference since it is inert under these conditions. A correction of 0.92 ppm was applied for protons. Variable-temperature measurements were calibrated against a methanol sample. Peak areas were obtained either by integration using the software of the operating system or by measurement with a planimeter. Chemical shifts are accurate to at least 0.01 ppm.

Titanium tetrachloride was purified by fractional distillation and stored in a container on the vacuum system. All other reagents were purified as previously described.[11,12] Samples were prepared by condensing known quantities of vapors into the NMR tube and sealing under vacuum except for the nonvolatile liquids mesitylene and methyl mesityl ketone. A weighed quantity of these materials was transferred to an NMR tube, closed by a high-vacuum stopcock, in a good-quality drybox. The tube was then mounted on the vacuum system and sample preparation completed. All samples were prepared in sulfur dioxide as solvent, and all concentrations are reported as mole fractions.

Table I. Chemical Shifts as a Function of Composition for the System $TiCl_4$–$(CH_3)_2O$ at −84 °C in SO_2

init concn[a]			chem shift, ppm				
				1:2			[trans]/
$TiCl_4$	$(CH_3)_2O$	ratio	1:1	trans	cis	$(CH_3)_2O$	[cis]
0.017 2	0.005 13	3.4:1	4.30				
0.007 23	0.004 94	1.5:1	4.20				
0.004 34	0.004 72	1:1.1		4.07	3.94		1.3
0.004 34	0.006 83	1:1.6		4.07	3.93		1.8
0.004 33	0.009 19	1:2.1		4.08	3.93		1.5
0.004 32	0.011 7	1:2.7		4.08	3.61		
0.004 31	0.014 1	1:3.3		4.06	3.44		
0	0.015					3.19	

[a] All concentrations in this and the following tables are reported as mole fractions.

Results and Discussion

Titanium tetrachloride reacts with dimethyl ether to give a 1:1 and two different 1:2 complexes. The 1:1 complex, whose methyl protons have a chemical shift of 4.30 ppm, is only observed when more than 1 equiv of $TiCl_4$ is nominally present in the sample. There is no information on its stereochemistry, and it may be a dimer or polymeric. The signal from the 1:2 complex at 4.07 ppm is assigned to the trans complex with octahedral geometry about titanium by analogy with similar chemical shift and exchange behavior of the analogous $SnCl_4$ complexes,[11] where the trans isomer has a signal at lower field and exchanges more slowly than the cis isomer. The signal from the 1:2 complex at 3.93 ppm is assigned to the cis complex. It exchanges rapidly on the NMR time scale at −84 °C with excess of uncomplexed ether. Results for samples of varying composition are presented in Table I. The signal at high field in the samples with a ratio of 1:2.7 and 1:3.3 is a weighted average from the cis isomer and free ether. Calculation of the expected shift for the averaged line of free ether and the complex agrees with that observed. At −74 °C, exchange between the cis and trans isomers, without excess ether, is sufficiently rapid that separate signals are no longer observed.

Positive identification of a ternary 1:1:1 complex of $TiCl_4$, dimethyl ether, and HCl in solution comes from the proton

(1) Issued as NRCC No. 23104.
(2) Loder, D. J.; Walker, K. E. U.S. Patent 2052889, 1936.
(3) Cullinane, N. M.; Chard, S. J.; Leyshon, D. M. *J. Chem. Soc.* **1952**, 4106–4108.
(4) Susz, B. P.; Lachavanne, A. *Helv. Chim. Acta* **1958**, *41*, 634–636.
(5) Hessett, B.; Perkins, P. G. *J. Chem. Soc. A* **1970**, 3229–3234.
(6) Sheldon, J. C.; Tyree, S. Y. *J. Am. Chem. Soc.* **1959**, *81*, 2290–2296.
(7) Susz, B. P.; Cassimatis, D. *Helv. Chim. Acta* **1961**, *44*, 943–955.
(8) Cassimatis, D; Gagnaux, P.; Susz, B. P. *Helv. Chim. Acta* **1960**, *43*, 424–433.
(9) Patai, S., Ed. "The Chemistry of the Acyl Halides"; Interscience: New York, 1972; Chapter 4.
(10) Bond, P. A.; Belton, W. E. *J. Am. Chem. Soc.* **1945**, *67*, 1691–1693.
(11) Tan, L. K.; Brownstein, S. *J. Org. Chem.* **1983**, 48, 3389–3393.
(12) Tan, L. K.; Brownstein, S. *J. Org. Chem.* **1983**, 48, 302–306.

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