Inorg. Chem. **1982**, *21*, 3494-3501

$-\Delta G_0 \approx E_s + u_f(R_c) - u_i(R_c) < 0$. For this to be possible, R_c must correspond to a considerable stretch of the Br–O bond, which in fact provides the dominating contribution to E_a, and the motion of the separated fragments must be restricted by a strong repulsive potential, so that $u_f'(R_c) >> u_i'(R_c)$. R_c is then the distance of closest approach of the two fragments, and $u_i(R_c)$ and $u_f(R_c)$ become reorganization energies along the mode R (the Br–O bond).

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Registry No. BrO_4^-, 16474-32-1; $[Fe(L–L)_3]^{2+}$, L–L = 2,2′-bipyridyl, 15025-74-8; $[Fe(L–L)_3]^{2+}$, L–L = 1,10-phenanthroline, 14708-99-7; $[Fe(L–L)_3]^{2+}$, L–L = 5-nitro-1,10-phenanthroline, 15245-50-8; $[Fe(L–L)_3]^{2+}$, L–L = 4,7-dimethyl-1,10-phenanthroline, 15226-33-2.

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Electron-Transfer Reactions of Copper(III)–Peptide Complexes with Hexacyanoferrate(II)

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The rate constants for the electron-transfer reactions of $Fe(CN)_6^{4-}$ with a series of copper(III)–peptide complexes vary from 2.6×10^5 M^{-1} s^{-1} to greater than 8×10^7 M^{-1} s^{-1}. The reactions proceed more slowly in the presence of alkali metal ions due to their association with $Fe(CN)_6^{4-}$. The reactions with $Cu^{III}(H_{-3}Aib_3a)$, where Aib_3a is di-α-aminoisobutyryl-α-aminoisobutyramide, permit the resolution of stability constants (M^{-1}, 25.0 °C) for $Fe(CN)_6^{4-}$ with alkali metal ions, Li^+ (16) ~ Na^+ (13) < K^+ (29) < Cs^+ (55), and redox rate constants (M^{-1} s^{-1}) for $Fe(CN)_6^{4-}$ (2.2×10^6) > $LiFe(CN)_6^{3-}$ (1.0×10^6) > $NaFe(CN)_6^{3-}$ (3.1×10^5) ≃ $KFe(CN)_6^{3-}$ (3×10^5) > $CsFe(CN)_6^{3-}$ (1.3×10^5). Most of the electron-transfer reactions with Cu(III) are 1–2 orders of magnitude faster than an outer-sphere mechanism predicts. This suggests a pathway in which cyanide bridges axially to the square-planar Cu(III) complexes facilitating the electron transfer from $Fe(CN)_6^{4-}$. The reaction products give evidence of a cyano bridge as quenching of the Cu(II)–peptide EPR signal occurs upon addition of $Fe(CN)_6^{3-}$. Bulky groups in the Cu(III)–peptide ligand serve to block the formation of the cyano bridge and give smaller electron-transfer rate constants, which are in agreement with an outer-sphere mechanism.

Introduction

Rapid electron-transfer reactions have been observed for copper(III, II)–peptide couples with several other redox couples.[1-4] Although the electrode potentials of the Cu(III, II) couples vary greatly with the peptide ligand (the values range from 1.02[5] to 0.37 V[6] vs. NHE), the self-exchange rate constant appears to be relatively insensitive to the nature of the coordinated peptide. Recently ^1H NMR line broadening was used[7] to determine directly the self-exchange rate constant for the $Cu^{III}(H_{-2}Aib_3)$–$Cu^{II}(H_{-2}Aib_3)^-$ complexes.[8] This value was in good agreement with values calculated from several Cu(III) peptide–Cu(II) peptide cross-exchange reactions by using the Marcus theory[9] and gave a self-exchange rate constant of 5×10^4 M^{-1} s^{-1} at 25 °C. The outer-sphere oxidation of ruthenium(II) ammine complexes[10] by Cu(III) peptides yield copper self-exchange rate constants that also are in good agreement with the NMR values and the values determined from the Cu(III)–Cu(II) cross reactions.

On the other hand, the very rapid reactions for the reduction[1] of Cu(III) peptides by $IrCl_6^{3-}$ and for the oxidation[4] of Cu(II) peptides by $IrCl_6^{2-}$ gave apparent self-exchange rate constants of 10^8 M^{-1} s^{-1} for the Cu(III, II) couples. Although these reactions show a Marcus correlation slope of 0.5, an inner-sphere mechanism with electron transfer occurring by a chloride bridge between Cu and Ir was proposed[1,4] to account for the 3 orders of magnitude increase in the apparent self-exchange rate constant.

In the present work the hypothesis of an inner-sphere electron-transfer mechanism for Cu(III, II) peptides is tested by using the reactions of $Fe(CN)_6^{4-,3-}$. The latter complexes have been shown in other reactions[11-13] to occur via a bridging cyano group as well as by outer-sphere electron transfer. The self-exchange rate constants are known[14,15] for $Fe(CN)_6^{3-,4-}$ so that the magnitude of the cross-reaction rate constants can be used to test for evidence of pathways more favorable than that expected from the Marcus correlation of the outer-sphere rate constants. The results indicate that the cyano group provides an inner-sphere bridge between iron and copper that is comparable to that found for the hexachloroiridate reactions.

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(8) Abbreviations used for the peptides: α-aminoisobutyryl, Aib; glycyl, G; alanyl, A; valyl, V; phenylalanyl, F; a designates a terminal amide group; H_{-n} refers to n deprotonated peptide nitrogens coordinated to the metal.
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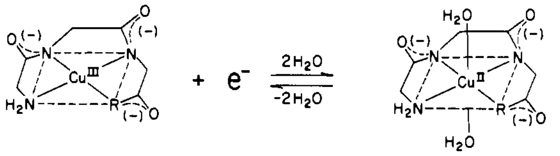
Table I. Spectral and Electrochemical Data[a,b] for Copper Peptide Complexes

complex	λ_{max}, nm	ϵ, M^{-1} cm^{-1}	$Cu^{II,III}$ $E°$, V	$E°_{reacn}$, V[c]
$Cu^{III}(H_{-3}Aib_3a)^0$ [d]	364	6900	0.370	−0.047
$Cu^{III}(H_{-3}G_2AibG)^-$ [d]	366	8000	0.520	0.103
$Cu^{III}(H_{-3}G_4)^-$	365	7400	0.630	0.213
$Cu^{III}(H_{-2}Aib_3)^0$ [e]	395	5200[d]	0.660	0.243
$Cu^{III}(H_{-3}A_4)^-$	375[f]	~7000	0.600	0.183
$Cu^{III}(H_{-3}V_4)^-$	365	~7000	0.510	0.093
$Cu^{III}(H_{-3}F_4)^-$	365	~7000	0.623[g]	0.206
$Cu^{III}(H_{-3}A_3G)^-$	365	~7000	0.530[g]	0.113
$Cu^{III}(H_{-3}AG_3)^-$	365	~7000	0.610	0.193
$Cu^{III}(H_{-3}VG_2a)^0$	365	~7000	0.610	0.193
$Cu^{III}(H_{-3}G_3a)^0$	365	7500	0.640	0.220
$Cu^{III}(H_{-3}G_3A)^-$	380[f]	~7000	0.688[g]	0.271

[a] $\mu = 0.1$ M ($NaClO_4$). [b] Reference 5. [c] For reaction consisting of $Cu^{III}L + Fe^{II}(CN)_6{}^{4-}$, see Results for discussion of the $Fe^{III}(CN)_6{}^{3-} + e^- \rightleftarrows Fe^{II}(CN)_6{}^{4-}$ couple, $E° = 0.417$ V vs. NHE. [d] Reference 6. [e] Kirksey, S. T., Jr.; Neubecker, T. A.; Margerum, D. W. *J. Am. Chem. Soc.* 1979, *101*, 1631. [f] Read, R., personal communication. [g] This work.

Reaction entropies for the copper(III, II)–peptide couples show that changes in axial solvent coordination occur with the change of oxidation state[16] as depicted in eq 1, where R can



(1)

be a carboxylate oxygen, a deprotonated amide nitrogen, or a deprotonated peptide nitrogen. Thus, the Cu(III) complexes can be approached readily by bridging ligands in the axial positions, and it is possible to displace the axial waters in the Cu(II) complexes. We present evidence in this work for a weak Cu^{II}(peptide)–$Fe^{III}(CN)_6{}^{3-}$ complex.

Experimental Section

High-purity peptides containing the amino acid group α-aminoisobutyric acid (Aib_3, Aib_3a, and G_2AibG) were synthesized in this laboratory by A. W. Hamburg. All other peptides used were of chromatographic purity as purchased (Biosynthetika, Oberdorf, Switzerland).

Solutions of the copper(II) complexes were prepared by reaction of $Cu(ClO_4)_2$ solutions with a 10% molar excess of peptide. The solutions were raised to pH 10.3, ensuring the formation of the fully deprotonated complex,[5,17] and electrolyzed to the corresponding Cu(III) complexes with use of a flow-through electrochemical cell held at a potential ~0.2 V > $E°$, as previously reported.[18] Table I gives the spectroscopic and electrochemical data for the complexes used in this study.

Reagent grade potassium hexacyanoferrate(II) was recrystallized once from water and dried for 6 h at 126 °C. The salt was standardized with Ce(IV) and found to have the formula $K_4Fe(CN)_6$. Care was taken to store the salt in an opaque, desiccated container.

A stock solution of $NaClO_4$ was prepared by neutralizing Na_2CO_3 with $HClO_4$ followed by gravimetric standardization. Solid $CsClO_4$ was prepared by precipitating the salt from a concentrated mixture of $NaClO_4$ and CsCl. All other chemicals were reagent grade. The reactions were carried out in room light that was passed through a Kodak 1A filter ($\lambda > 580$ nm) to avoid photochemical decomposition of the Cu(III) complexes.[6]

Kinetic measurements were made by observing the absorbance of the Cu(III) peptide at the λ_{max} of each complex with a Durrum stopped-flow spectrophotometer interfaced to a Hewlett-Packard 2108 computer. The reactions were buffered at pH ~5 (acetate–acetic acid), adjusted to an ionic strength of 0.10 M ($NaClO_4$) and thermostated at 25.0 ± 0.1 °C unless otherwise stated. Each reaction was conducted under pseudo-first-order conditions and was found to be strictly first order. The reactions all followed the rate law

Table II. Rate Data for the Reaction of $Cu^{III}(H_{-3}Aib_3a) + Fe^{II}(CN)_6{}^{4-}$ [a]

$10^6 \times$ $[Cu^{III}L]$, M	$10^4 \times$ $[Fe^{II}(CN)_6{}^{4-}]$, M	$10^2 \times$ $[OAc]_T$, M	pH	k_{obsd},[b] s^{-1}
4.0	0.201	1.0	5.24	19.3 ± 6[c]
4.0	0.502	1.0	5.24	55.9 ± 0.4[c]
4.0	1.00	1.0	5.24	112 ± 2[c]
4.0	1.51	1.0	5.24	164 ± 1[c]
4.0	2.01	1.0	5.24	224 ± 5[c]
10.7	0.012	1.0	5.22	11 ± 3[d]
4.0	0.502	1.0	4.81	55.7 ± 0.6
4.0	0.502	1.0	5.24	55.9 ± 0.4
4.0	0.502	1.0	5.68	56.4 ± 1.4
5.0	0.512	0.10	5.24	56.9 ± 0.7
5.0	0.512	0.50	5.15	55.5 ± 0.4
5.0	0.512	1.0	5.14	56.2 ± 0.5

[a] $\mu = 0.1$ M($NaClO_4$) at 25.0 ± 0.1 °C. [b] Standard deviation is from three replicate runs. [c] Least-squares regression gives $k_{obsd} = ((1.12 \pm 0.02) \times 10^6\ M^{-1}\ s^{-1})[Fe^{II}(CN)_6{}^{4-}] - (1.7 \pm 2.1)\ s^{-1}$. [d] This gives a second-order rate constant of $(1.0 \pm 0.3) \times 10^6\ M^{-1}\ s^{-1}$.

$$-d[Cu^{III}L]/dt = k[Cu^{III}L][Fe^{II}(CN)_6]_T \tag{2}$$

where $[Fe^{II}(CN)_6]_T$ is the total of all Fe(II) species in solution.

Cyclic voltammetry was carried out with a three-electrode system consisting of a glassy carbon electrode, a saturated calomel reference electrode, and a platinum wire auxiliary electrode, all controlled by a Bioanalytical Systems CV-1A instrument.

Electron paramagnetic resonance spectra (EPR) of millimolar copper(II) peptide solutions were measured at room temperature (~21 °C) with a Varian E-109 X-band EPR system modulated at 100 kHz. The data were acquired and manipulated by a Varian E935 data acquisition system. Room-temperature spectra were obtained after each small addition of $Fe^{III}(CN)_6{}^{3-}$ to a solution of copper(II) peptide that was constantly circulated through an aqueous cell by a peristaltic pump. The ionic strength of the Cu(II) solution was adjusted to 3.0 M with NaCl so that the ionic strength would be constant upon addition of aliquots of 0.50 M $Fe(CN)_6{}^{3-}$. Changes in the ionic strength were found to affect the intensity of the EPR signal, presumably due to variation in the solvent dielectric losses.

Results

Reaction of $Cu^{III}(H_{-3}Aib_3a)$ and $Fe^{II}(CN)_6{}^{4-}$. In basic solution the reaction is thermodynamically unfavorable as given in eq 3. However, in slightly acidic solution the rapid acid

$$Cu^{III}(H_{-3}Aib_3a) + Fe^{II}(CN)_6{}^{4-} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} Cu^{II}(H_{-3}Aib_3a)^- + Fe^{III}(CN)_6{}^{3-} \tag{3}$$

dissociation of the Cu(II) complex, eq 4, causes overall loss

$$Cu^{II}(H_{-3}Aib_3a)^- \xrightarrow[k_d]{H^+} Cu^{2+}(aq) + Aib_3a \tag{4}$$

of Cu(III). At pH 5.2 the reaction is first order in the loss of the Cu(III) complex and the observed first-order rate constant varies linearly with the total hexacyanoferrate(II) concentration.

The rate law from the reactions in eq 3 and 4, with the assumption of a steady-state concentration in the Cu(II) complex, is given in eq 5. The rate of acid dissociation of another peptide complex, copper(II) tetraglycine, depends not only on the pH but on the concentration of general acid as

$$\frac{-d[Cu^{III}(H_{-3}Aib_3a)]}{dt} = \frac{k_1k_d[Cu^{III}(H_{-3}Aib_3a)][Fe^{II}(CN)_6]_T}{k_{-1}[Fe^{III}(CN)_6{}^{3-}] + k_d} \tag{5}$$

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[17] Hamburg, A. W.; Margerum, D. W., to be submitted for publication.
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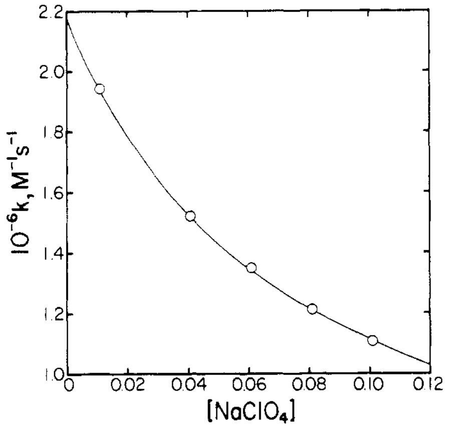


Figure 1. Dependence of the reaction rate of $Cu^{III}(H_{-3}Aib_3a)$ and $Fe^{II}(CN)_6^{4-}$ upon the concentration of $NaClO_4$ added. Conditions are as given in Table III.

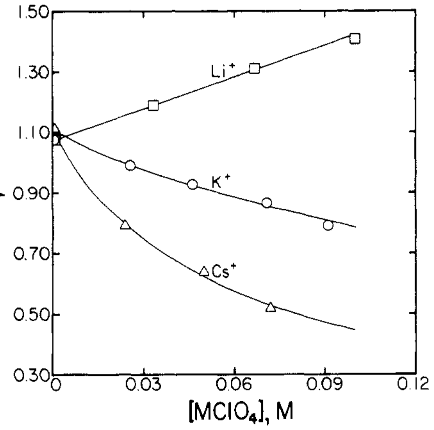


Figure 2. Dependence of the reaction rate of $Cu^{III}(H_{-3}Aib_3a)$ and $Fe^{II}(CN)_6^{4-}$ upon the concentration of various perchlorate salts at a constant ionic strength with $NaClO_4$: Li^+ (□); K^+ (○); Cs^+ (△). Conditions are as given in Table III.

well.[19] Such dependencies of the rate of the reaction in eq 4 would also be expected. However, as can be seen from the data in Table II, the rate of loss of the Cu(III) complex is not affected by changing the pH or by varying the acetic acid–acetate content and there is no evidence of $Fe^{III}(CN)_6^{3-}$ inhibition. This indicates that $k_d >> k_{-1}[Fe^{III}(CN)_6^{3-}]$, so that the rate law in eq 5 reduces to that in eq 6. Thus, the

$$\frac{-d[Cu^{III}(H_{-3}Aib_3a)]}{dt} = k_1[Cu^{III}(H_{-3}Aib_3a)][Fe^{II}(CN)_6]_T \qquad (6)$$

rate-limiting step is the electron transfer and not the dissociation of the Cu(II) complex. The value of the k_1 is (1.12 ± 0.02) × 10^6 M^{-1} s^{-1} at 25.0 °C in 0.10 M $NaClO_4$.

Effect of Perchlorate Salt Content on the Reaction Rate. Since a neutral Cu(III) complex is the reactant in eq 3, the rate might be expected to be independent of the salt concentration and the ionic strength. However, as Figure 1 shows, the second-order rate constant does vary with the concentration of $NaClO_4$. This effect is ascribed to the Na^+ cation because at constant ionic strength with $NaClO_4$ the addition of $LiClO_4$, $KClO_4$, or $CsClO_4$ also affects the rate constants as seen in Figure 2 and Table III. Similar effects were noted in the determination of the self-exchange rate constant of the ferricyanide–ferrocyanide couple.[14,15] However, since both reactants were charged, a mixture of primary and secondary salt effects was observed in these studies. In the present system only secondary effects are present. The data in all cases suggest that cations associate with the highly charged $Fe^{II}(CN)_6^{4-}$, causing changes in reactivity.

Table III. Effect of Perchlorate Salt Concentration on the Rate of Reaction for $Cu^{III}(H_{-3}Aib_3a)$ and $Fe^{II}(CN)_6^{4-}$ [a]

M^+	$[MClO_4]$, M	$[NaClO_4]$, M	pH[b]	$10^{-5}k$, M^{-1} s^{-1} [c]
		0.0109	5.50	19.4 ± 0.8
		0.0409	5.31	15.2 ± 0.3
		0.0609	5.29	13.5 ± 0.1
		0.0808	5.26	12.1 ± 0.2
		0.101	5.28	11.1 ± 0.2
Li^+		0.110	5.2	10.8 ± 0.2
	0.0333	0.0767	5.2	11.9 ± 0.1
	0.0667	0.0433	5.2	13.1 ± 0.2
	0.1000	0.0100	5.2	14.1 ± 0.2
K^+		0.101	5.19	10.8 ± 0.1
	0.0255	0.0760	5.16	9.89 ± 0.08
	0.0457	0.0560	5.19	9.28 ± 0.08
	0.0709	0.0310	5.16	8.64 ± 0.08
	0.0911	0.0110	5.18	7.90 ± 0.09
Cs^+		0.101	5.21	11.1 ± 0.1
	0.0240	0.0770	5.22	7.96 ± 0.11
	0.0500	0.0510	5.22	6.36 ± 0.09
	0.0720	0.0290	5.21	5.15 ± 0.08

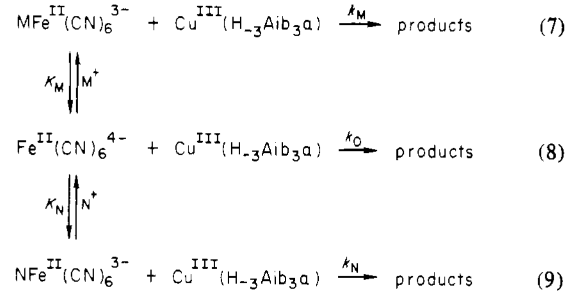
[a] 20.5 °C. [b] 1.0 mM NaOAc-HOAc buffer. [c] $k_{obsd}/[Fe^{II}(CN)_6]_T$; standard deviation is that of three replicate runs.

Table IV. Rate and Equilibrium Constants[a] for Various Fe(II) Species

species	K_M^{II}, M^{-1}	k_M, M^{-1} s^{-1}
$Fe^{II}(CN)_6^{4-}$		(2.18 ± 0.01) × 10^6
$LiFe^{II}(CN)_6^{3-}$	16 ± 1	(1.02 ± 0.03) × 10^6
$NaFe^{II}(CN)_6^{3-}$	13.2 ± 0.4	(3.1 ± 0.3) × 10^5
$KFe^{II}(CN)_6^{3-}$	29 ± 5	(3 ± 1) × 10^5
$CsFe^{II}(CN)_6^{3-}$	55 ± 8	(1.3 ± 0.8) × 10^5

[a] At 25.0 °C and pH 5.2 with 1.0 mM sodium acetate buffer.

The scheme shown in eq 7–9 is proposed for the Cu(III) reactions.



Under pseudo-first-order conditions in which $Cu^{III}(H_{-3}Aib_3a)$ is the limiting reagent, we obtain the rate law shown in eq 10 and 11, where $[Fe^{II}(CN)_6]_T$ refers to the total

$$-d[Cu^{III}(H_{-3}Aib_3a)]/dt = k_{obsd}[Cu^{III}(H_{-3}Aib_3a)] \qquad (10)$$

$$k_{obsd} = \left(\frac{k_0 + K_M k_M[M] + K_N k_N[N]}{1 + K_M[M] + K_N[N]}\right)[Fe^{II}(CN)_6]_T \qquad (11)$$

Fe^{II} species in solution. The data of Figure 1, in which only $NaClO_4$ was present as an added salt, were analyzed by a nonlinear regression algorithm. The resolved constants were k_0 = (2.18 ± 0.01) × 10^6 M^{-1} s^{-1}, k_{Na} = (3.1 ± 0.3) × 10^5 M^{-1} s^{-1}, and K_{Na} = 13.2 ± 0.4 M^{-1}. From these values, the data obtained with two added cations (Table III) could be analyzed linearly, and the results are summarized in Table IV.

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Table V. Cyclic Voltammetry Data for $Cu^{II,III}(H_{-3}Aib_3a)^{0,1-}$ and $Fe(CN)_6^{4-,3-}$ as a Function of the Cation Used

$Fe(CN)_6^{4-,3-}$		$Cu^{II,III}(H_{-3}Aib_3a)^{0,1-}$	
salt[a]	$E°$,[b] V	salt[a]	$E°$,[c] V
LiCl	0.4161	$LiClO_4$	0.365
NaCl	0.4161	$NaClO_4$	0.370
KCl	0.4244	$KClO_4$	0.372
RbCl	0.4334	$RbClO_4$	
CsCl		$CsClO_4$	0.372
$NaClO_4$	0.4164		
$NaClO_4$	0.417[c]		

[a] [MX] = 0.10 M. [b] Reference 21; precision ±0.5 mV. [c] This work; precision ±5 mV.

Table VI. Rate Data for the Reaction of $Cu^{II}(H_{-3}Aib_3a)^-$ and $Fe^{III}(CN)_6^{3-}$ [a]

$10^5 \times [Fe(CN)_6^{3-}]$, M	k_{obsd}, s^{-1}	$10^5 \times [Fe(CN)_6^{3-}]$, M	k_{obsd}, s^{-1}
1.07	45.2 ± 0.9	4.26	171 ± 9
2.13	88.9 ± 0.6	5.33	219 ± 19
3.20	132 ± 2		

[a] Conditions: $\mu = 0.1$ M ($NaClO_4$); pH 10.4 with 0.01 M carbonate; $T = 25.0$ °C. Least-squares regression gives $k_{obsd} = ((4.03 \pm 0.06) \times 10^6\ M^{-1}\ s^{-1})[Fe^{II}(CN)_6^{3-}] + (2.2 \pm 2.2)\ s^{-1}$.

The value of K_M for potassium ion of 29 M^{-1} is in excellent agreement with the value reported by Chlebek and Lister[20] of 31 M^{-1} ($\mu = 0.1$ M). It has been suggested that multiple cations can associate with the $Fe(CN)_6^{4-}$;[14] however, the data do not appear to suggest multiple associations in the present case.

The observed trends in reactivity can be explained on the basis of the electrode potentials of the copper and iron couples. As seen in Table V, the cation used to control the ionic strength has a much larger effect on the electrode potential of the $Fe(CN)_6^{4-,3-}$ couple than the $Cu^{III,II}(H_{-3}Aib_3a)^{0,-}$ couple. In addition the iron potentials are not dependent on the anions used.[21] The electron-transfer reactions in eq 7–9 are more rapid as the potentials calculated for each cation from Cs^+ to Li^+ are less negative.

Reaction of $Cu^{II}(H_{-3}Aib_3a)^-$ and $Fe^{III}(CN)_6^{3-}$. The reaction was carried out at pH 10.4 to ensure that the fully deprotonated Cu(II) complex, eq 12, was present (log K_H = 7.97

$$Cu^{II}(H_{-3}Aib_3a)^- + H^+ \underset{}{\overset{K_H}{\rightleftharpoons}} Cu^{II}(H_{-2}Aib_3a) \qquad (12)$$

± 0.01[17]). The reaction was found to be first order in the loss of Cu(II), and the observed rate constant varied linearly with $[Fe^{III}(CN)_6^{3-}]$ as shown in Table VI. The resolved second-order rate constant k_{-1} (see eq 3), corrected for the small amount of Cu(II) complex that is not triply deprotonated (~0.4%), is (4.04 ± 0.06) × $10^6\ M^{-1}\ s^{-1}$. Knowledge of the forward and reverse rate constants allows the determination of the equilibrium constant from $K_{kin} = k_1/k_{-1} = 0.28$. The equilibrium constant calculated from the measured copper and iron electrode potentials given in Table I, $K_{ec} = 0.16$, is in fair agreement with the kinetic value.

Temperature Dependence of the Reaction Rates. Rate constants for the reduction of $Cu^{III}(H_{-3}Aib_3a)$ and $Cu^{III}(H_{-3}G_2AibG)^-$ from 8 to 33 °C are reported in Table VII along with the rate constant for $Cu^{III}(H_{-2}Aib_3)$ at 8.5 °C. At each temperature for the reduction of $Cu^{III}(H_{-3}G_2AibG)$, the rate law in eq 2 was confirmed. The resolved activation parameters for the two Cu(III) reactions with $Fe^{II}(CN)_6^{4-}$ are as follows: $Cu^{III}(H_{-3}Aib_3a)$, $\Delta H^* = 8.3 \pm 0.3$ kcal/mol, $\Delta S^* = -3 \pm 1$ cal deg^{-1} mol^{-1}; $Cu^{III}(H_{-3}G_2AibG)^-$, $\Delta H^* = 5.63 \pm 0.01$ kcal/mol, $\Delta S^* = -7.6 \pm 0.3$ cal deg^{-1} mol^{-1}. On the basis of the influence of cations on the reaction rate, the activation parameters must be considered as composites of rate and equilibrium temperature dependences. However, the cation stability constant for Na^+ is small (13.2), and the reactivity of $NaFe(CN)_6^{3-}$ is smaller than the free species so that the contributions of this equilibrium to the activation parameters will be small (~18%).

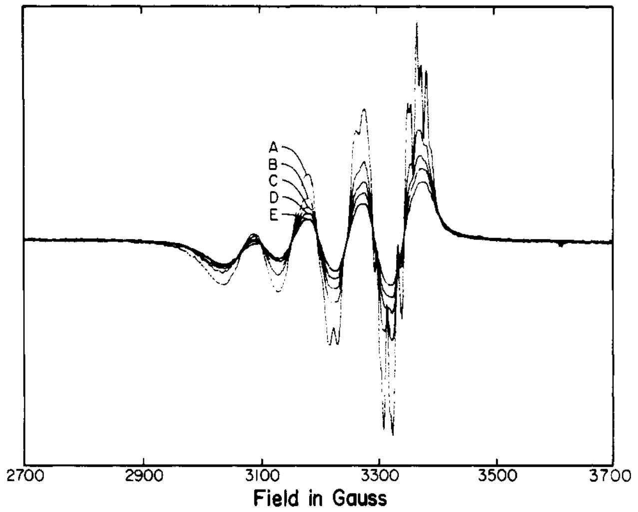

Figure 3. EPR spectra of a $Cu^{II}(H_{-2}Aib_3)^-$ solution containing increasing amounts of $Fe^{III}(CN)_6^{3-}$. Concentration of $Fe^{III}(CN)_6^{3-}$: (A) 0; (B) 0.0588 M; (C) 0.105 M; (D) 0.143 M; (E) 0.188 M. Each spectrum was corrected for dilution before being plotted. Conditions: $[Cu^{II}Aib_3]$ = 2.67 mM, stock $[Fe^{III}(CN)_6^{3-}]$ = 0.500 M, pH 8.5, total volume 15.0 mL initially, μ = 3.0 M with NaCl, T = 21 °C, and microwave frequency 9.40 GHz.

Interactions of $Fe(CN)_6^{3-}$ with Cu(II) Peptides. The room-temperature EPR spectrum of $Cu^{II}(H_{-2}Aib_3)^-$ is shown in Figure 3, curve A. The EPR signal intensity is reduced by the addition of $Fe(CN)_6^{3-}$, curves B–E. Two features can be noted upon increasing the concentration of $Fe(CN)_6^{3-}$. First, the metal hyperfine structure (mhf) decreases in intensity without broadening. Second, the ligand superhyperfine lines (lshf) show significant broadening such that the resolved structure is lost after the first addition of $Fe(CN)_6^{3-}$, curve B.

The loss of intensity of the mhf lines indicates a direct metal–metal interaction in which the spins of the copper and iron couple antiferromagnetically to produce an EPR-silent adduct, eq 13. The lack of broadening of the mhf line suggests

$$Cu^{II}(H_{-2}Aib_3)^- + Fe^{III}(CN)_6^{3-} \underset{k_d}{\overset{k_f}{\rightleftharpoons}} [Cu^{II}(H_{-2}Aib_3)\cdot Fe^{III}(CN)_6]^{4-} \qquad (13)$$

that exchange of Cu(II) centers is slow on the time scale for the relaxation of these resonances. However, the loss of the lshf structure upon addition of $Fe(CN)_6^{3-}$ suggests a broadening mechanism is important in these transitions.

Analysis of the lshf line widths using a slow-exchange model[22] can give information on the rate of an exchange-broadening process. A crude estimate of the lshf linewidth is ~5 G, which is equivalent to ~14 MHz (assuming the g value is ~2.0) and specifies a relaxation time (τ) of 7 × 10^{-8} s. Since broadening of the lshf is seen at the lowest $Fe(CN)_6^{3-}$ concentration (0.0588 M), it is possible to calculate a minimum second-order broadening rate, with the assumption of an Fe-

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Table VII. Temperature-Dependent Kinetic Data for the Reactions[a] of Copper(III) Peptides with $Fe^{II}(CN)_6^{4-}$

complex	$10^5[Fe^{II}(CN)_6^{4-}]$, M	T, °C	k_{obsd}, s^{-1}	$10^{-6}k$, M^{-1} s^{-1}
$Cu^{III}(H_{-3}G_2AibG)^-$ [b]	0.538	8.5	32 ± 1	5.46 ± 0.07
	1.61	8.5	91 ± 1	
	3.23	8.5	177 ± 5	
	0.538	16.3	38 ± 1	7.4 ± 0.1
	1.61	16.3	119 ± 17	
	0.538	24.4	50 ± 1	9.9 ± 0.2
	1.61	24.4	159 ± 13	
$Cu^{III}(H_{-3}Aib_3a)^-$ [c]	5.16	9.8	26.3 ± 0.8	0.51 ± 0.02
	5.16	15.9	37 ± 1	0.72 ± 0.03
	5.16	20.5	46 ± 1	0.88 ± 0.03
	5.16	26.9	62 ± 2	1.21 ± 0.03
	5.16	32.9	87 ± 4	1.69 ± 0.07
$Cu^{III}(H_{-2}Aib_3)$[d]	1.61	8.5	300 ± 15	20 ± 1

[a] $\mu = 0.1$ M ($NaClO_4$); pH = 5.2 with 1.0 mM OAc_T; $[Cu^{III}L] \approx 1 \times 10^{-6}$ M. [b] $\lambda_{obsd} = 250$ nm; resolved activation parameters are $\Delta H^{\ddagger} = 5.63 \pm 0.01$ kcal mol^{-1}, $\Delta S^{\ddagger} = -7.6 \pm 0.3$ cal deg^{-1} mol^{-1}. [c] Resolved activation parameters are $\Delta H^{\ddagger} = 8.3 \pm 0.3$ kcal mol^{-1}, $\Delta S^{\ddagger} = -3 \pm 1$ cal deg^{-1} mol^{-1}. [d] $\lambda_{obsd} = 285$ nm.

Table VIII. Summary of Rate Data and Resolved Rate Constants for the Reaction of Hexacyanoferrate(II) with Copper(III) Peptide Complexes[a]

peptide	$10^5[Fe^{II}(CN)_6^{4-}]$, M	pH	k_{obsd}, s^{-1}	$10^{-6}k$, M^{-1} s^{-1} [b]
$Cu^{III}(H_{-3}V_4)^-$	1.05	5.04	2.64 ± 0.11	0.261 ± 0.002
	2.10	5.04	5.31 ± 0.09	
	10.5	5.05	27.4 ± 0.7	
	21.0	5.06	53.8 ± 0.6	
	31.4	5.06	82.2 ± 0.5	
$Cu^{III}(H_{-3}A_3G)^-$	1.11	5.18	40.3 ± 0.5	7.8 ± 0.2
	2.21	5.18	91.9 ± 1.5	
	6.63	5.18	259 ± 7	
$Cu^{III}(H_{-3}A_4)^-$	0.542	5.2	54.3 ± 0.6	9.8 ± 0.2
	1.08	5.2	105 ± 2	
	2.16	5.2	195 ± 15	
$Cu^{III}(H_{-3}AG_3)^-$	0.542	5.04	185 ± 21	35 ± 4
$Cu^{III}(H_{-3}F_4)^-$	1.11	5.17	18.6 ± 0.7	2.9 ± 0.1
	2.21	5.17	35.7 ± 0.2	
	6.63	5.17	94 ± 4	
	11.1	5.18	166 ± 10	
$Cu^{III}(H_{-3}G_4)^-$	0.542	5.2	~300	~60
$Cu^{III}(H_{-3}G_3A)^-$	0.499	5.20	~400	~80
$Cu^{III}(H_{-3}VG_2a)$	0.555	5.19	281 ± 14	51 ± 3
$Cu^{III}(H_{-3}G_3a)$	0.260	5.20	>200	>80
$Cu^{III}(H_{-2}Aib_3)$	1.65	5.2	285 ± 15	40[d]

[a] Conditions are $\mu = 0.1$ M($NaClO_4$), $T = 25.0$ °C, 0.01 M acetate buffer, and $[Cu^{III}] \approx 1 \times 10^{-6}$ M. [b] Least-squares regression values where possible. [c] 8.5 °C. [d] Extrapolated to 25 °C by using the average $\Delta S^{\ddagger}$ of −5 cal deg^{-1} mol^{-1}.

(III) exchange mechanism and by using the relationship $\tau^{-1} = k_{ex}$. The calculated rate constant is $k_{ex}/[Fe^{III}(CN)_6^{3-}] > 2 \times 10^8$ M^{-1} s^{-1}. Electron exchange, eq 14, could be a cause

$$Cu^{II}(H_{-2}Aib_3)^- + Fe^{III}(CN)_6^{3-} \underset{k_1}{\overset{k_{-1}}{\rightleftarrows}} Cu^{III}(H_{-2}Aib_3) + Fe^{II}(CN)_6^{4-} \quad (14)$$

for line broadening, but on the basis of the value of the equilibrium constant, $K_e = 1.28 \times 10^4$ and the forward rate constant, $k_1 = 4.0 \times 10^7$ M^{-1} s^{-1}, the calculated value for the reverse rate constant, $k_{-1} = 3.13 \times 10^3$ M^{-1} s^{-1}, is too slow to account for the broadening on the EPR time scale.

A calculated rate constant of 5×10^8 M^{-1} s^{-1} for the axial substitution of copper(II) peptides in their reaction with $IrCl_6^{2-}$ agreed with the experimental observations for this system.[4] The similarity of this rate constant and the exchange rate constant above suggests that the formation and dissociation of the copper–iron adduct, eq 13, is a case of concentration broadening due to spin exchange.[23] Caution must be exercised when this type of assignment is made since the high concentrations of $Fe^{III}(CN)_6^{3-}$ can give rise to dipole–dipole broadening. However, this mechanism is usually less effective compared to the spin-exchange broadening.[23]

There was some question as to the coordination site of the $Fe^{III}(CN)_6^{3-}$ in the adduct. The square plane of $Cu^{II}(H_{-2}Aib_3)^-$ contains three strong nitrogen donors and a carboxylate group. Conceivably, ferricyanide could substitute for either the equatorial carboxylate or an axial water. To resolve this, we titrated a second complex with ferricyanide. This complex, $Cu^{II}(H_{-3}G_4)^{2-}$, has four strong nitrogen donors in the square plane and has only axial sites available for coordination. Axial coordination of ferricyanide is indicated as the same behavior of the EPR signal is noted for both the Aib_3 and the G_4 complexes. Stability constants were calculated on the basis of the reaction in eq 13 for $Cu^{II}(H_{-2}Aib_3)^-$ and $Cu^{II}(H_{-3}G_4)^{2-}$ and were found to be 8.1 ± 0.5 and $\lesssim 10$ M^{-1}, respectively. The values were corrected for small decreases in the Cu(II) and Fe(III) concentrations due to the equilibrium expressed in eq 14.

Reaction of the Series of Cu(III) Complexes with $Fe^{II}(CN)_6^{4-}$. The data in Table VIII represent the reductions of the remaining Cu(III) peptide complexes of Table I. Sufficient data were taken to confirm the adherence to the rate law in eq 2 for most of the reactions; however, a concentration dependence was precluded in some cases due to the very rapid

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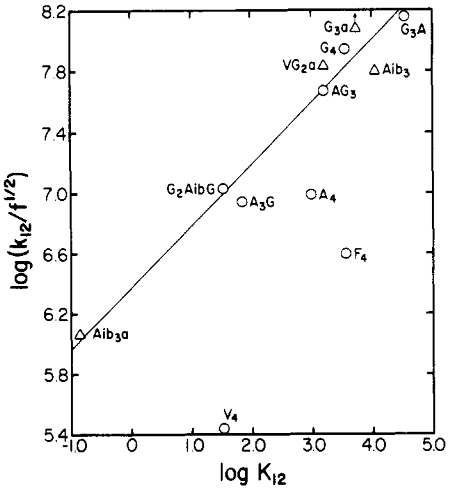

Figure 4. Marcus correlation for the reactions of $Cu^{III}(H_{-x}L)^{0,1}$ (△) or $Cu^{III}(H_{-x}L)^{1-,2-}$ (○) with $Fe^{II}(CN)_6^{4-}$ (25 °C, $\mu = 0.10$ M ($NaClO_4$)). The solid line is the linear regression: $\log(k_{12}/f^{1/2}) = (0.41 \pm 0.03) \log K_{12} + (6.4 \pm 0.1)$. Values not included in the analysis are those for the Cu(III) complexes of A_4, V_4, and F_4; see text.

rates observed. The latter cases are single-point determinations in which the rate law of eq 2 is assumed. Rather large error limits occur for the very rapid rates measured since very small absorbance changes (0.01 unit) are observed. Table VIII summarizes the resolved second-order rate constants. For the reaction involving $Cu^{III}(H_{-3}G_3a)$ only a lower limit for the rate constant could be given. Figure 4 shows a Marcus correlation for many of the reactions and indicates that the A_4, F_4, and V_4 complexes fall off this correlation.

Discussion

The reactions of copper peptide complexes and of $Fe(CN)_6^{4-,3-}$ are known to occur by both inner-sphere and outer-sphere mechanisms.[1,4,10,11,24] The Marcus theory is used here in an attempt to identify the operative mechanism in the copper–iron cross reactions.

In its simplest form the Marcus theory can predict the rate constant for the cross reaction (k_{12}) on the basis of the self-exchange rate constant for each partner (k_{11}, k_{22}) and the cross-reaction equilibrium constant (K_{12}), as in eq 15 and 16,

$$k_{12} = (k_{11}k_{22}K_{12}f)^{1/2} \tag{15}$$

$$\log f = (\log K_{12})^2/[4 \log (k_{11}k_{22}/Z^2)] \tag{16}$$

where Z is the collision frequency of 10^{11} M^{-1} s^{-1}. The self-exchange rate for both partners in the copper–iron cross reaction have been determined by a number of methods.

The rate constant for $Cu^{II,III}(H_{-2}Aib_3)$ exchange has been determined by ^1H NMR to be 5.5×10^4 M^{-1} s^{-1}.[7] Published as well as preliminary data[7,10] suggest that a large number of Cu–peptide complexes all have similar exchange rates, in the range of $(0.4–5.5) \times 10^4$ M^{-1} s^{-1}. These results were determined from cross reactions among different copper–peptide complexes. We have chosen to use the value 5×10^4 M^{-1} s^{-1} as a representative value for the copper(III, II) peptide self-exchange rate constant.

The self-exchange of $Fe(CN)_6^{4-,3-}$ appears to be more complicated as Campion et al.[14] in their isotopic exchange reactions and Shporer et al.[15] in an ^{14}N NMR study have found significant catalysis of the rate by cations. Neither study has determined the rate in 0.1 M $NaClO_4$ as needed for this work. However, the rate dependence upon K^+ concentration as well as the temperature dependence has been resolved,[14] which allows the extrapolation of the rate data from 0.1 to 25 °C in 0.1 M K^+. The calculated value is 9.7×10^3 M^{-1} s^{-1}. At much higher concentrations the rates have been determined[15] for both Na^+ and K^+ media (1.75 M, $k_{Na} = 5.8 \times 10^4$ M^{-1} s^{-1}, $k_K = 7.9 \times 10^4$ M^{-1} s^{-1}, ratio = 0.73). Thus, a good estimate can be calculated by correcting the value in 0.1 M K^+ by the ratio of the rates with Na^+ and K^+, $k = 9.67 \times 10^3 \times 0.73 = 7.1 \times 10^3$ M^{-1} s^{-1}. This is in good agreement with the reported value of 7.3×10^3 M^{-1} s^{-1} at $\mu = 0.1$ Na_2SO_4 (0.033 M Na_2SO_4).[25]

Before the self-exchange rates can be used to predict the rates of the cross reactions, further considerations are necessary. As stated in eq 15 and 16, Marcus' theory assumes that the work terms required to bring the reactants together and separate the products are very similar or negligible for the self-exchange and cross-exchange processes so as to cancel out in the treatment. For the reaction of Cu(III) peptides with $Fe^{II}(CN)_6^{4-}$ this assumption is not valid. In the $Fe(CN)_6^{4-,3-}$ exchange the large negative charges of the ions give rise to large electrostatic work terms that are not present in the cross reactions or in the self-exchange of the Cu(III, II) complexes. The predicted rate can be corrected for electrostatic effects as shown in eq 17–25,[26,27] where single and double asterisks

$$\Delta G_{11}^* = -RT \ln (k_{11}/Z) \tag{17}$$

$$\Delta G_{22}^* = -RT \ln (k_{22}/Z) \tag{18}$$

$$\Delta G_{11}^{**} = \Delta G_{11}^* - w_{11} \tag{19}$$

$$\Delta G_{22}^{**} = \Delta G_{22}^* - w_{22} \tag{20}$$

$$\Delta G_r^\circ = \Delta G_{12}^\circ + w_{21} + w_{12} \tag{21}$$

$$\Delta G_{12}^{**} = \frac{\Delta G_{11}^{**} + \Delta G_{22}^{**}}{2} + \frac{\Delta G_r^\circ(1 + \alpha)}{2} \tag{22}$$

$$\alpha = \frac{\Delta G_r^\circ}{4(\Delta G_{11}^{**} + \Delta G_{22}^{**})} \tag{23}$$

$$\Delta G_{12}^* = \Delta G_{12}^{**} + w_{12} \tag{24}$$

$$k_{12}^{\text{calcd}} = Ze^{-\Delta G/RT} \tag{25}$$

correspond to the observed and corrected free energies of activation. The work terms have been calculated by using the Debye–Hückel expression,[28] eq 26, where D is the absolute

$$w = Z_1Z_2e^2/[Da(1 + \kappa a)] \tag{26}$$

solvent dielectric, κ is the reciprocal ionic layer thickness, and a is the sum of the reactant radii. The radii were determined by using eq 27,[28] where d_x, d_y, and d_z are the molecular di-

$$r = \tfrac{1}{2}(d_xd_yd_z)^{1/3} \tag{27}$$

ameters along the three axes estimated from CPK space-filling models. The diameters were in crude agreement with those measured from the recent crystal structure determination of $Cu^{III}(H_{-2}Aib_3)$.[29] The major difference in the radii of the copper complexes for +3 and +2 oxidation states is due to the change in coordinated water, see eq 1. The radius for $Fe(CN)_6^{4-,3-}$ has been estimated to be 4.5 Å.[30] Table IX lists the calculated work terms, the approach radii, and the predicted rate constants for the cross reactions studied. In most cases the observed rate constant is much larger than predicted. When calculating the work terms, we were concerned about the charges of the iron couple since cation association was noted. Parallel calculations were performed with $Fe(CN)_6^{4-,3-}$ and $MFe(CN)_6^{3-,2-}$ as the reacting species and indicated the predicted rates were slower for the cation complex. This reflects the importance of the repulsion of the products in the

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Table IX. Calculated[a] and Observed Reaction Rates for Copper(III) Peptides

complex	r, Å		work, kcal			$10^{-6}k_{\text{calcd}}$, $M^{-1}\ s^{-1}$	$10^{-6}k_{\text{obsd}}$, $M^{-1}\ s^{-1}$
	Cu^{III}	Cu^{II}	w_{11}	w_{12}	w_{21}		
$Cu^{III}(H_{-3}Aib_3a)$	4.3	4.7	0	0	0.71	0.043	1.12
$Cu^{III}(H_{-3}VG_2a)$	3.6	4.6	0	0	0.72	4.76	51
$Cu^{III}(H_{-3}G_3a)$	3.4	4.3	0	0	0.75	6.50	$\geqslant$80
$Cu^{III}(H_{-2}Aib_3)$	4.3	4.7	0	0	0.71	9.37	40
$Cu^{III}(H_{-3}V_4)^-$	5.2	5.2	0.39	0.87	1.30	0.270	0.26
$Cu^{III}(H_{-3}G_2AibG)^-$	3.5	4.7	0.55	1.13	1.41	0.268	10.1
$Cu^{III}(H_{-3}A_3G)^-$	4.1	4.9	0.49	1.04	1.37	0.344	7.84
$Cu^{III}(H_{-3}A_4)^-$	4.1	4.9	0.49	1.04	1.37	1.17	9.78
$Cu^{III}(H_{-3}AG_3)^-$	3.8	4.9	0.51	1.09	1.37	1.34	35
$Cu^{III}(H_{-3}F_4)^-$	6.6	6.6	0.27	0.71	1.06	2.35	2.92
$Cu^{III}(H_{-3}G_4)^-$	3.6	4.7	0.55	1.13	1.41	1.80	~60
$Cu^{III}(H_{-3}G_3A)^-$	3.6	4.7	0.55	1.13	1.41	4.70	~80
$Cu^{II}(H_{-3}Aib_3a)^{-}$ [b]	4.3	4.7	0	0.71	0	0.304	4.04

[a] Parameters used were $k_{11} = 5 \times 10^4\ M^{-1}\ s^{-1}$, $k_{22} = 7 \times 10^3\ M^{-1}\ s^{-1}$, $r_{Fe} = 4.5$ Å, $E_{Fe}{}^{\circ} = 0.42$ V vs. NHE, and $w_{22} = 2.91$ kcal/mol. [b] Cu(II) complex reacting with $Fe^{III}(CN)_6{}^{3-}$.

predicted rate constants. We chose to use 4–, 3– as the charges for the predictions in Table IX since this tended to give an *upper limit* to the predicted rate constants, as does the use of the copper(II, III) upper limit self-exchange rate constant of $5 \times 10^4\ M^{-1}\ s^{-1}$.

Mechanism of Electron Transfer. A simple outer-sphere electron-transfer process has been eliminated in favor of an inner-sphere mechanism for the following reasons. First, the inability of Marcus' theory to predict rapid enough rates is taken as evidence for a more facile pathway. The self-exchange of the copper peptide would need to be $\sim 10^8\ M^{-1}\ s^{-1}$ for the predicted rates to align with the observed, in accord with an outer-sphere mechanism. This is nearly 3 orders of magnitude larger than independently observed.

Second, it has been suggested[31] that the decrease in the EPR signal of $Cu^{II}G_2$ in the presence of $Fe^{III}(CN)_6{}^{3-}$ at liquid-nitrogen temperature is due to antiferromagnetic coupling between Cu(II) and Fe(III) by a cyano bridge (i.e., Fe^{III}–CN–Cu^{II}). The exact Cu(II) coordination could not be determined since an equatorial and an axial site were available. The formation of an adduct between $Fe^{III}(CN)_6{}^{3-}$ and bis(ethylenediamine)copper(II) was observed by using room-temperature EPR.[32] The square plane of the Cu(II) complex is coordinatively saturated and therefore requires an axial interaction. A stability constant of $\sim 10^3\ M^{-1}$ was estimated for this case where electrostatic interactions were favorable. This can be compared to a stability constant of 8.1 M^{-1} at room temperature for $Cu^{II}(H_{-2}Aib_3)^-$ with $Fe^{III}(CN)_6{}^{3-}$. Also the broadening of the lshf lines by spin exchange suggests the axial substitution on $Cu^{II}(H_{-2}Aib_3)^-$ is quite rapid. While the formation of the Cu^{II}–Fe^{III} adduct does not prove conclusively that this process is intimately involved in the electron-transfer reactions, it does show that such an interaction is favorable and that the antiferromagnetic coupling exhibited indicates sufficient orbital overlap is attained for a direct electron transfer to occur.

Third, the cyano group is expected to be a better bridging ligand than Cl^- (which has been proposed to bridge in the $IrCl_6{}^{3-,2-}$ and Cu(III, II) peptide system), since it is more basic in nature with a pK_a for ferrocyanide of ~ 4[33] as compared to $IrCl_6{}^{2-}$, which was found to be unprotonated at pH 4.15.[34] The weak affinity of Cu(II) peptides for the coordination of nitrogen-based ligands in the axial position has already been shown for substituted pyridines.[35] In addition, ferrocyanide has been shown to undergo electron transfer by cyano group bridging in a number of systems,[11-13] and in general cyanide is noted for bridging capabilities in the electron-transfer reactions of cobalt(II, III).[36]

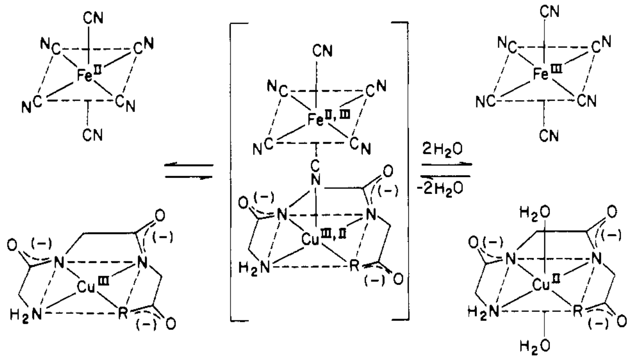

Figure 5. Proposed mechanism of electron transfer in which the transition state (in brackets) involves a cyano bridge between Cu(III) and Fe(II). Solvation of Cu(II) is thought to occur after break up of the transition state.

Finally the presence of both inner- and outer-sphere mechanisms can best explain the behavior of the Cu(III) complexes of V_4 and F_4 in their reactions with $Fe^{II}(CN)_6{}^{4-}$, on the basis of steric considerations. As pointed out in the $IrCl_6{}^{2-}$ study,[4] considerable steric crowding occurs if all the α-carbon substituents of a tetrapeptide are oriented toward the same side of the copper plane. Rotation of the fourth residue of the tetrapeptide relieves this crowding but places the α substituent in such a position as to block the opposite axial site of copper. Indications are that for Ni(II) peptide complexes (which have the same structure as Cu(III) peptides, d^8, square planar) the side chains of the chelates prefer to be situated over the axial metal site as opposed to being swung away from the metal.[37] This implies that for the large hydrophobic groups of V_4, F_4, and possibly A_4, both axial sites are sterically blocked to incoming molecules. The relatively good agreement of the Marcus predictions for $Cu^{III}(H_{-3}F_4)^-$ and $Cu^{III}(H_{-3}V_4)^-$ suggests that the blocking is complete and in essence the reaction is an outer-sphere process. It is not surprising that the remaining Cu(III) reactions show a Marcus correlation; see Figure 4. Marcus has shown[38] that such a correlation could be expected for cases of strong-overlap electron transfer such as the inner-sphere reactions suggested here. The slope of the correlation (0.43 ± 0.03) is slightly less

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than the expected value of 0.5; however, this appears to be true in other cases as well.[1,39]

On the basis of the above rationale, we propose that the electron transfer is proceeding through a ferrocyano nitrogen bridging axially to the square-planar Cu(III) complex in the transition state, as shown in Figure 5. As indicated in eq 1, Cu(III) has no coordinated water and must gain two waters on going to Cu(II). Judging from the small negative values of $\Delta S^{\ddagger}$ found, the gain of waters probably occurs after the transition state for the following reasons. We expect ~9 cal $\mathrm{deg^{-1}\ mol^{-1}}$ will be lost in bringing together the two metal centers, and perhaps slightly more in forming the inner-sphere bridge. A small gain in $\Delta S^{\ddagger}$ is possible due to delocalization of the Fe charge over the copper complex, which gives rise to a less organized solvent structure. Overall, this indicates a slightly negative $\Delta S^{\ddagger}$, and addition of H_2O to copper in the transition state (−7.6 cal $\mathrm{deg^{-1}\ mol^{-1}}$ contribution to $\Delta S^{\ddagger}$ [7,16]) would produce an entropy value too negative compared to the observed $\Delta S^{\ddagger}$ to be probable and suggests the mechanism in Figure 5.

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Registry No. $\mathrm{Fe(CN)_6^{3-}}$, 13408-62-3; $\mathrm{Cu^{III}(H_{-3}Aib_3a)}$, 82495-22-5; $\mathrm{Cu^{III}(H_{-3}G_2AibG)^-}$, 82495-23-6; $\mathrm{Cu^{III}(H_{-3}G_4)^-}$, 57692-61-2; $\mathrm{Cu^{III}(H_{-2}Aib_3)}$, 69990-31-4; $\mathrm{Cu^{III}(H_{-3}A_4)^-}$, 68628-66-0; $\mathrm{Cu^{III}(H_{-3}V_4)^-}$, 62959-93-7; $\mathrm{Cu^{III}(H_{-3}F_4)^-}$, 82495-24-7; $\mathrm{Cu^{III}(H_{-3}A_3G)^-}$, 82495-25-8; $\mathrm{Cu^{III}(H_{-3}AG_3)^-}$, 69088-03-5; $\mathrm{Cu^{III}(H_{-3}VG_2a)}$, 62801-40-5; $\mathrm{Cu^{III}(H_{-3}G_3a)}$, 62801-36-9; $\mathrm{Cu^{III}(H_{-3}G_3A)^-}$, 82495-26-9.

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Axial Coordination of Monodentate Ligands with Nickel(III) Peptide Complexes

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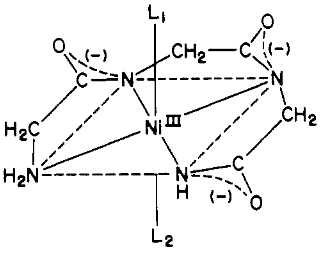
Stability constants are determined by an electrochemical method for axial coordination of monodentate nitrogen ligands to nickel(III) peptide complexes in aqueous solution. The stability constants at 25 °C vary from 1100 to 50 M^{-1} (in the order imidazole > $NH_3 \simeq N_3^-$ > pyridine) but are relatively independent of the nature of the peptide. The substitution is too fast to observe by stopped-flow methods, and a lower limit for the axial water exchange rate constant is estimated as $k_{H_2O} > 4 \times 10^6\ s^{-1}$. There are no reactions observed with the corresponding nickel(II) peptides. Displacement of water from the second axial site of nickel(III) occurs in frozen aqueous solutions with ammonia but not at room temperature. The diglycylethylenediamine (DGEN) complex, $\mathrm{Ni^{III}(H_{-2}DGEN)^+}$, adds H^+ and Cl^- to give one or two axially coordinated Cl^- in frozen aqueous solution (123 K), but the complexes are too weak to be detected at room temperature.

Introduction

Nickel(II) promotes ionization of peptide and amide hydrogens upon complexation by oligopeptides.[1] Coordination of deprotonated peptide nitrogens stabilizes the trivalent oxidation state of nickel, and the reduction potentials in aqueous solution for a variety of nickel(III, II) peptide couples have been determined.[2] Studies of the temperature dependence[3] of the electrode potentials indicate that the nickel(II) peptide complexes are not axially solvated, in contrast to the nickel(III) forms. Electron paramagnetic resonance studies[4,5] show that the nickel(III) peptides such as $\mathrm{Ni^{III}(H_{-3}G_3a)}$[6] (**1**) have a tetragonally distorted octahedral geometry, with solvent molecules occupying the axial sites and an approximately square-planar arrangement of the peptide donors. The EPR studies presented evidence for axial substitution by ammonia in frozen aqueous glasses to form both mono- and diammine adducts. Even very low ammonia concentrations resulted in the formation of complexes such as $\mathrm{Ni^{III}(H_{-3}G_3a)NH_3}$ in the frozen state, giving the appearance of a very strong complex in aqueous solution.[5] However, the present work shows that the ammonia complexes in aqueous solution are relatively weak and are many orders of magnitude less stable than estimated from the composition of the solutions before they are frozen.



1a, $L_1 = L_2 = H_2O$
b, $L_1 = NH_3$, $L_2 = H_2O$

Axial coordination of anionic ligands such as halides and sulfate to nickel(III) macrocyclic complexes has been recently reported.[7-10] Stability constants range from about 50 M^{-1} for Br^- to more than 10^3 M^{-1} for SO_4^{2-}. The rates of axial substitution have been examined as well. The corresponding complexes are not observed with the nickel(III) peptides.

Measurement of equilibrium constants for axial coordination of ammonia, imidazole, and other nitrogen ligands to nickel(III) peptides is complicated by protonation of the nitrogen

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[6] Abbreviations used: G_3a, triglycinamide; G_4, tetraglycine; A_4, tetraalanine; A_3, trialanine; G_2Aa, diglycylalaninamide; Aib, α-aminoisobutyryl; DGEN, diglycylethylenediamine. The subscript in $\mathrm{Ni(H_{-n}P)}$ refers to the number of deprotonated peptide or amide nitrogens coordinated to the metal ion.

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