Registry No. PTA, 99924-19-3; PTA-NH_3, 16455-68-8; PTA-OH_2, 17524-19-5; PTA-OH, 97732-33-7; PTA-ImH, 99924-20-6; PTA-Im, 99924-21-7; PTA-4-PyH, 99924-25-1; PTA-4-Py, 99924-26-2; PTA-pyrimidine, 99924-22-8; PTA-2-pyrimidone (O), 99924-23-9; PTA-2-pyrimidone (N), 99924-24-0; PTA-guanine (N7), 99924-27-3; PTA-guanine (O6), 99924-28-4; PTA-guanine (N3), 99924-29-5; PTA-adenine (N1), 99924-30-8; PTA-adenine (N3), 99924-31-9; PTA-adenine (N7), 99924-32-0; PTA-cytosine (N3), 99924-33-1; PTA-cytosine (O2), 99924-34-2; PTA-thymine (O2), 99924-35-3; PTA-thymine (O4), 99924-36-4.

Supplementary Material Available: Tables showing atomic charges and coordinates (8 pages). Ordering information is given on any current masthead page.

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Azolate Complexes of Nitrosyl(protoporphyrin IX dimethyl esterato)iron(II)

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Nitrosyl(protoporphyrin IX dimethyl esterato)iron(II) (Fe(PPIXDME)(NO)) complexes with various azolates as a trans axial ligand have been prepared in solution, and their EPR and electronic spectra have been measured at room temperature and at 77 K. The apparent EPR line shape of Fe(PPIXDME)(NO) complexes with azolates resembled that of the complexes with neutral azoles, while significant differences were found in EPR parameters. The basicity of the coordinated azolates is estimated from the EPR g values of the azolate complexes on the basis of the approximately linear relationship between g values and the basicity ($pK_a(BH^+)$) of azoles. The Soret band in the electronic spectra of Fe(PPIXDME)(NO) complexes with azolates was red-shifted compared to those of the azole complexes. These results are discussed in relation to the dissociation of the $N_\delta H$ proton in proximal histidyl imidazole in hemoproteins.

Introduction

The imidazole group of histidine residues is coordinated axially to heme iron in the majority of hemoproteins. The hydrogen bonding of the axial imidazole $N_\delta H$ proton to amino acid residues of the polypeptide chain leads either to fractional deprotonation or to complete deprotonation or imidazolate formation.[1] It has been suggested that such histidyl imidazolate is present in several hemoproteins.[2-5] Both the ferrous and ferric porphyrin complexes as model systems for hemoproteins have been investigated in order to clarify the differences between axial imidazole (ImH) and imidazolate (Im^-) in bonding ability to heme iron.[6-15] These studies have demonstrated that the imidazolate has greater σ-donor ability than the imidazole. However, the magnitude of change in basicity from imidazole to imidazolate has not yet been shown.

In preceding papers, we have reported EPR, IR, and electronic spectral studies on nitrosyl(protoporphyrin IX dimethyl esterato)iron(II) (Fe(PPIXDME)(NO)) complexes with various N-, O-, and S-donor bases (B) as an axial ligand trans to a nitrosyl group.[16-20] It was shown that these spectral parameters are dependent upon the electronic and stereochemical properties of the axial ligands, and in particular, the g values and NO stretching frequencies (ν_{NO}) in the complexes with unhindered imidazoles and pyridines vary linearly with the basicity of the base ($pK_a(BH^+)$).[21] During the course of these studies, we have found that Fe(PPIXDME)(NO) complexes with azolates are formed by the reaction of NO with the systems consisting of (protoporphyrin IX dimethyl esterato)iron(II) complexes with various azoles and tetraalkylammonium hydroxide. The present work reports on attempts to estimate the basicity of the azolates from the EPR g values of the complexes thus formed and to elucidate the bond strength of the iron to axial ligands.

Experimental Section

Materials and Methods. Fe(PPIXDME)Cl and Fe(PPIXDME)(NO) were prepared as described before.[22,23] Nitric oxide, purchased from Takachiho Trading Co., was passed through a KOH column to remove higher nitrogen oxides. The azoles were obtained commercially. The liquid bases were distilled by flowing N_2 under reduced pressure, and the solid bases were recrystallized or sublimed. All the solvents were dried and distilled by usual methods. The solvents and liquid bases were deoxygenated by bubbling with pure N_2 prior to use. Tetramethylammonium hydroxide (2.7 M) and tetrabutylammonium hydroxide (0.40 M) in methanol were purchased from Eastman Kodak Co. and Tokyo Chemical Industry, respectively. All other chemicals used were obtained as the best available grade and were used without further purification.

EPR measurements were carried out on a JES-ME-3X spectrometer with 100-kHz field modulation at about 20 °C and at 77 K, which was calibrated with a Takeda-Riken frequency counter Model TR-5211A and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical powder (g = 2.0036) and

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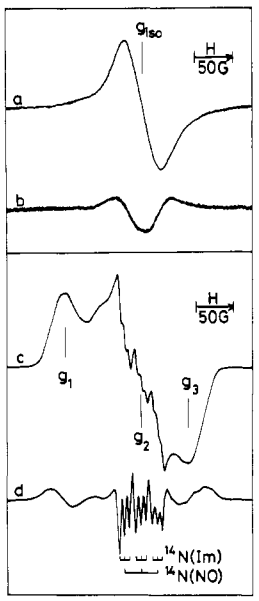

Figure 1. EPR spectra for the Fe(PPIXDME)(NO) complex with imidazolate: (a) first- and (b) second-derivative display at room temperature; (c) first- and (d) second-derivative display at 77 K. g_{iso} = 2.012; g_1 = 2.068, g_2 = 2.0032, and g_3 = 1.965. Instrument settings: modulation frequency and amplitude, 100 kHz and 2 G; microwave frequency, 9.4450 GHz at room temperature and 9.1743 GHz at 77 K; power, 10 mW.

Mn(II) in MgO (ΔH_{3-4} = 86.9 G) as standards. The second derivative display was obtained by the use of 80-Hz field modulation. The electronic absorption spectra were recorded on a Shimadzu MPS-5000 spectrophotometer at about 20 °C.

Sample Preparation. The complexes with azoles were prepared by dissolving Fe(PPIXDME)(NO) (5 mM) and azole in appropriate solvent under N_2 atmosphere, unless otherwise stated.

The complexes with azolates were prepared by the reaction of NO as follows. The reaction of NO was carried out in a Thunberg-type tube with an optical cuvette or with an EPR tube. The solutions containing Fe(PPIXDME)Cl, azole, and tetraalkylammonium hydroxide in dimethyl sulfoxide or dimethylacetamide were carefully degassed in the Thunberg tube by repeated freezing and thawing in vacuo. Then the solutions were equilibrated with NO gas at slightly below 1 atm. After the solution was allowed to stand for 1–2 h, EPR and electronic spectra were measured. The concentrations of Fe(PPIXDME)Cl, azole, and tetraalkylammonium hydroxide in EPR samples were 7–10 mM, 0.07–0.3 M, and 0.2–0.7 M, respectively; those in electronic spectral samples were 0.01–0.03 mM, 0.4 M, and 0.4 M, respectively.

Results and Discussion

Preparation of Azolate Complexes. The addition of hydroxide to the solution containing Fe(PPIXDME)Cl and imidazoles results in the preferential deprotonation of the coordinated imidazoles as described previously:[13]

$$\text{Fe(PPIXDME)Cl} + \text{ImH} \rightleftarrows [\text{Fe(PPIXDME)(ImH)}_2]^+\text{Cl}^-$$

$$[\text{Fe(PPIXDME)(ImH)}_2]^+ \overset{\text{OH}^-}{\rightleftharpoons} [\text{Fe(PPIXDME)(Im)}_2]^-$$

The $[Fe(PPIXDME)(Im)_2]^-$ species can react with excess NO to form $[Fe(PPIXDME)(NO)(Im)]^-$:

$$[\text{Fe(PPIXDME)(Im}_2)]^- \overset{\text{NO}}{\rightleftharpoons} [\text{Fe(PPIXDME)(NO)(Im)}]^-$$

In the course of the reaction, the iron(III) can be reduced to iron(II) by NO. This is a typical case of reductive nitrosylation,[24] which has been also found in the NO reaction of methemoglobin.[25]

Spectral Properties. The EPR spectra of $[Fe(PPIXDME)(NO)(Im)]^-$ in dimethyl sulfoxide at room temperature and at 77 K are shown in Figure 1. The spectrum at 77 K exhibited the line shape characteristic of randomly oriented systems with rhombic symmetry and the existence of three g values. Its g_2 absorption, which can be assigned to the g_z absorption,[26] exhibited a well-resolved hyperfine structure of a triplet of triplets. This hyperfine structure is originated from the hyperfine interactions of the unpaired electron with both ^{14}N nuclei of the NO group (the coupling constant, A_1) and the trans axial ligand (A_2), arising from the delocalization of the unpaired electron to the trans axial ligand.

Table I. EPR Parameters of Nitrosyl(protoporphyrin IX dimethyl esterato)iron(II) Complexes with Imidazoles and Imidazolates at Room Temperature[a]

base	$pK_a(BH^+)$[b]	g_{iso}
Im^-[c]		2.012
NMeIm[d]	7.33	2.021
ImH[e]	6.95	2.021
5ClNMeIm[d]	4.75	2.024

[a] About 20 °C. See footnote *a* of Table II for abbreviations. [b] References 27 and 29. [c] In dimethyl sulfoxide solution containing Me_4NOH. [d] In neat liquid base.[18] [e] In acetonitrile.[18]

The apparent EPR line shapes of $[Fe(PPIXDME)(NO)(Im)]^-$ complex at room temperature and at 77 K (Figure 1) resemble that of the Fe(PPIXDME)(NO)(ImH) complex (Figure 2 of ref 19). On the other hand, there are significant differences in EPR parameters of these complexes (Tables I and II). (The g_2 value was determined from the central line position of nine hyperfine lines in the second derivative display. The average A_1 and A_2 values are shown in Table II.) It has been shown in nitrosyliron(II) porphyrin complexes with imidazole derivatives as a trans axial ligand that the g_{iso} and ν_{NO} values at room temperature decrease with an increase in $pK_a(BH^+)$ value.[18] The g_{iso} value of the complex with imidazolate is markedly smaller compared with those for complexes with imidazole derivatives (Table I), suggesting that imidazolates have larger pK_a values. At 77 K, the three g values (g_1, g_2, and g_3) of the complexes with azolate are smaller than those of the complexes with azole (Table II). The g_2 (or g_z) values of the azolate complexes are closer to a free-spin value than those of the azole ones, which indicates that the interaction of an unpaired electron with the d_{z^2} orbital for the former is weaker. The A_1 values, which reflect the unpaired electron density at the nitrogen nucleus of the NO group, are slightly larger in the azolate complexes than in azole ones. These results suggest that the azolate complexes have a weaker iron to NO bond than the azole ones and have a stronger iron to trans axial ligand bond.

The EPR spectrum of the system with Fe(PPIXDME)(NO) and neutral tetrazole at 77 K exhibited the line shape of five-coordinate (Fe(PPIXDME)(NO)) species with a trace of six-coordinate species. Thus, the $pK_a(BH^+)$ value or σ-bonding ability of a tetrazole may be so small that the EPR spectrum of six-coordinate species can not be obtained. When the systems with pyrazoles and indazoles with a dissociable NH proton at the position adjacent to donor nitrogen were allowed to react with NO in the presence of tetraalkylammonium hydroxide, the product exhibited EPR spectra and parameters similar to those of systems with neutral bases. The reason that azolate complexes were not formed in the systems with these bases remains ambiguous.

The electronic spectrum of Fe(PPIXDME)(NO)(NMeIm) was almost independent of the solvent and the method of preparation (Table III). As shown in Table III, the Soret band for $[Fe(PPIXDME)(NO)(Im)]^-$ is red-shifted compared to that for Fe(PPIXDME)(NO)(NMeIm). Thus, the deprotonation of coordinated imidazole in the nitrosyl iron(II) porphyrin complex results in red shifts of the Soret band. This result is consistent with that obtained for carbonyliron(II) porphyrin complexes with

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Table II. EPR Parameters of Nitrosyl(protoporphyrin IX dimethyl esterato)iron(II) Complexes with Azoles and Azolates at 77 K[a]

no.	bases[b]	$pK_a(BH^+)$[c]	g values			axial coupling const, G	
			g_1	g_2	g_3	A_1	A_2
			Imidazoles				
1	NAcIm[d]	3.6[e]	2.077	2.0049	1.977	21.8	7.1
2	5ClNMeIm	4.75[f]	2.078	2.0048	1.98	21.6	7.0
3	BzImH[g]	5.53	2.081	2.0057	1.98	21.6	6.2
4	4PhImH[h]	6.00	2.072	2.0045	1.97	22.0	6.8
5	ImH[d]	6.95	2.072	2.0040	1.971	21.7	6.9
6	NBzlIm	7.0[i]	2.074	2.0043	1.98	21.6	6.8
7	NMeIm[d]	7.33	2.074	2.0041	1.971	21.5	6.9
8	4MeImH[d]	7.52	2.071	2.0038	1.970	21.9	7.0
9	$1,2Me_2Im$[j]	7.85[f]	2.077	2.0045	1.977	21.6	6.7
10	2MeImH[d,h]	7.86	2.079	2.0044	1.98	21.6	6.2
11	$1,2,4,5Me_4Im$[h]	9.2[k]	2.073	2.0045	1.98	22	7
			Pyrazoles and Indazoles				
12	PzH	2.47	2.080	2.0054	1.98	21.5	7.3
13	3MePzH	3.56	2.078	2.0053	1.98	21.5	7.4
14	IzH[h]	1.22	2.079	2.0057	1.98	21.0	6.5
15	$6NH_2IzH$[h]	4.02	2.076	2.0053	1.98	21.5	6.8
			Triazole				
16	1,2,4TazH[h]	2.30	2.074	2.0052	1.97	21.8	6.6
			Thiazole				
17	Thiazole	2.53	2.080	2.0057	1.98	21.4	6.5
			Azolates				
18	$BzIm^-$[l]		2.074	2.0035	1.97	23.2	6.6
19	$4PhIm^-$[m]		2.066	2.0031	1.963	22.3	6.9
20	Im^-[m]		2.068	2.0032	1.965	22.4	6.9
21	$4MeIm^-$[m]		2.068	2.0032	1.966	22.2	6.8
22	$1,2,4Taz^-$[m]		2.070	2.0036	1.977	22.2	6.8
23	$Tetraz^-$[l]		2.071	2.0040	1.974	22.1	7.3

[a] Abbreviations used: NAcIm, 1-acetylimidazole; 5ClNMeIm, 5-chloro-1-methylimidazole; BzImH, benzimidazole; ImH, imidazole; NBzlIm, 1-benzylimidazole; NMeIm, 1-methylimidazole; PzH, pyrazole; IzH, indazole; 1,2,4TazH, 1,2,4-triazole; $BzIm^-$, benzimidazolate; Im^-, imidazolate; $1,2,4Taz^-$, 1,2,4-triazolate; $Tetraz^-$, tetrazolate. [b] In chloroform unless otherwise noted. [c] Reference 27 unless otherwise noted. [d] Reference 16. [e] Reference 28. [f] Reference 29. [g] In dimethylacetamide. [h] In acetone. [i] Reference 30. [j] Reference 19. [k] Estimated from ref 28 and 29. [l] In dimethylacetamide solution containing Me_4NOH. [m] In dimethyl sulfoxide solution containing Bu_4NOH.

Table III. Electronic Spectral Data of Nitrosyl(protoporphyrin IX dimethyl esterato)iron(II) Complexes with 1-Methylimidazole and Imidazolate at Room Temperature[a]

complex	absorpn max, nm (ϵ, mM^{-1} cm^{-1})		
	γ(Soret)	β	α
Fe(PPIXDME)(NO)-(NMeIm), A[b]	418.5 (118)	546.5 (11.5)	576.5 (10.6)
Fe(PPIXDME)(NO)-(NMeIm), B[c]	417.5 (132)	545 (13.1)	576 (12.4)
[Fe(PPIXDME)(NO)-(Im)]$^-$[d]	423	547	579

[a] About 20 °C. See footnote *a* of Table II for abbreviations. [b] Reference 20. The spectrum obtained from the solution of Fe(PPIXDME)(NO) in NMeIm–benxene mixture. [c] The spectrum obtained by the reaction of $[Fe(PPIXDME)(NMeIm)_2]^+$ with NO in dimethylacetamide. [d] The spectrum obtained by the reaction of $[Fe(PPIXDME)(Im)_2]^-$ with NO in Me_4NOH–dimethylacetamide mixture. $\alpha/\beta = 0.83$.

anionic ligands,[6] though the magnitude of the red shifts from imidazole to imidazolate for the latter complex (610 cm^{-1}) is larger than that for the former (310 cm^{-1}). It has been demonstrated that the Soret band positions of nitrosyliron(II) porphyrin complexes are almost independent of the π-bonding ability of an axial ligand trans to the nitrosyl group.[20] Accordingly, it is likely that this red shift of the Soret band is correlated with the increase in basicity (σ-bonding ability) of the trans axial ligand that results from the deprotonation of coordinated imidazole.[6]

Basicity of Coordinated Azolates. We have demonstrated that the g_2 (or g_z) value in the EPR spectra (at 77 K) of Fe(PPIXDME)(NO) complexes with unhindered imidazoles and pyridines almost linearly decreases with an increase in the $pK_a(BH^+)$ value of these trans axial ligands, and thus the iron to ligand bond strength increases with a σ-bonding ability of the ligand.[16] Such an approximately linear relationship can be expected to exist

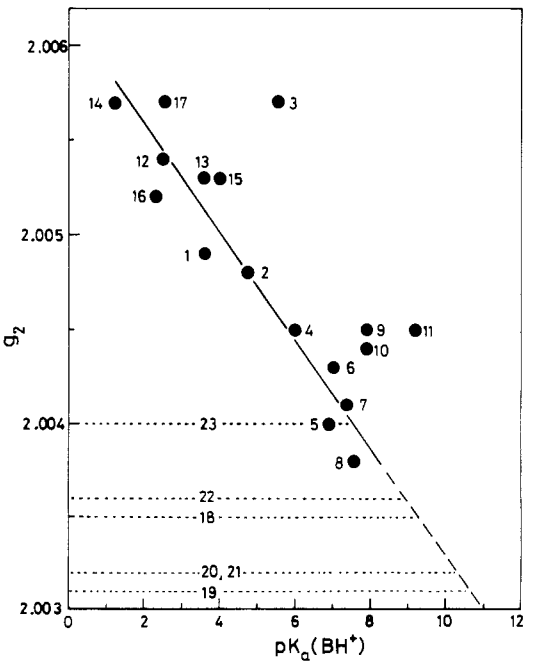

Figure 2. Relationships between the g_2 values (at 77 K) of Fe(PPIXDME)(NO) complexes with azoles and the $pK_a(BH^+)$ values of the azoles. Numbers refer to bases in Table II. The straight line was obtained by the least-squares method for the plots of unhindered azoles. The dashed horizontal lines indicate the position of the g_2 value of bases from **18**–**23**.

between the g_2 values of the azole complexes and the $pK_a(BH^+)$ values of the azoles. Plots of the g_2 values in Table II against the $pK_a(BH^+)$ values are illustrated in Figure 2, in which the straight line was drawn by the least-squares method for the plots of unhindered azoles. The plots of hindered imidazoles (**3**, **9**, **10**, and **11**) are separately located to the upper side of the straight line, independent of their $pK_a(BH^+)$ values, which can correspond to the weakening of the iron to ligand bond due to the steric interaction with the porphyrin core.

The $pK_a(B)$ value of the coordinated azolates can be estimated from the g_2 values of the azolate complexes on the extrapolation of the straight line in Figure 2. The estimated $pK_a(B)$ values are 7-8 for tetrazolate, 8.5-9.5 for 1,2,4-triazolate and benzimidazolate, and 10-11 for imidazolate, 4-methylimidazolate, and 4-phenylimidazolate. Thus, the benzimidazole of a hindered imidazole and the tetrazole and 1,2,4-triazole of a weak base are transformed into a strong base on deprotonation of N_1H, and the deprotonation in unhindered imidazoles leads to a pK_a shift of 3-4 units. It is interesting that the magnitude of this increase in pK_a value at the N_3 position of the unhindered imidazoles is comparable to that of the shift in pK_a value for deprotonation at N_1H from free imidazole (14.44)[31] to coordinated imidazole in ferric porphyrin complex (10.4)[32] and metmyoglobin (10.34).[31]

The deprotonation of coordinated azole N_1H can weaken the iron to NO bond as described above, accompanying an increase in the basicity of donor nitrogen. The weakening of iron to NO bond may facilitate the dissociation of nitrosyl ligand. This is consistent with the result that the reaction of Fe(PPIXDME)(NO)(base) $\rightleftarrows$ Fe(PPIXDME)(base)$_2$ + NO proceeds to the right as the iron to NO bond strength in Fe(PPIXDME)(NO)(base) complex decreases.[20] Accordingly, it is probable that the deprotonation of proximal imidazole $N_\delta H$ in hemoproteins enhances the reactivity of the trans axial position, which coincides with the previous suggestions.[3,6,14]

Registry No. **2**, 85200-22-2; **3**, 100082-70-0; **4**, 100082-71-1; **5**, 71016-02-9; **6**, 100082-72-2; **11**, 100082-73-3; **12**, 100082-74-4; **13**, 100082-75-5; **14**, 100082-76-6; **15**, 100082-77-7; **16**, 100082-78-8; **17**, 85200-21-1; **18**, 100082-79-9; **19**, 100082-80-2; **20**, 100082-81-3; **21**, 100082-82-4; **22**, 100082-83-5; **23**, 100082-84-6; Fe(PPIXDME)Cl, 15741-03-4; Fe(PPIXDME)(NO), 58357-23-6.

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Kinetics of Ternary Complex Formation: The (Adenosine 5′-triphosphato)nickel(II) + 2,2′-Bipyridine System

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The kinetics of formation of mixed-ligand complexes containing nickel(II), 2,2′-bipyridine, and adenosine 5′-triphosphate were studied by stopped-flow spectroscopy at 15 °C. A single relaxation effect was observed in the near-UV region. The pH and concentration dependencies of this effect were modeled most completely by three interconnected ternary formation steps. These steps correspond to the ternary complex formation of Ni(ATPH)(bpy), Ni(ATP)(bpy) and HONi(ATP)(bpy). The formation rate constants were found to be 1.9×10^3, 4.3×10^3, and 2.2×10^5 M^{-1} s^{-1} respectively. The magnitudes of these constants are interpreted in terms of statistical effects, labilization of inner-sphere water molecules, and chelation effects.

Introduction

Considerable interest has been focused on the thermodynamics and kinetics of ternary metal complexes because of the role these complexes play in biological systems. Although many biological systems that require a metal ion also require enzymes and cofactors, much simpler systems may serve to investigate fundamental metal-ligand interactions.

As a result of previous studies on binary and ternary systems, several factors have been identified that determine ternary complex formation rates: (1) the magnitude of the outer-sphere metal-ligand association constant, K_{os} (which varies greatly as a function of the association distance, ligand charge, metal charge, and bulk ionic strength);[1] (2) the rate of dissociation of inner-sphere water molecules (which is characteristic of a given metal but is dependent on the nature and number of bound ligands);[2-9] (3) the number of sites available for reaction;[10] (4) the preferred orientation of the available sites for a given incoming ligand.[11-13]

This paper presents an analysis of the formation rate constants for the ternary system Ni|ATP|bpy[14] for several concentrations over the pH range 4.5-8.5. Previous studies, with few exceptions,[15] have investigated the kinetics of ternary systems over a comparatively narrow pH range. We also present kinetic data for the component system Ni|bpy. Although this binary system has been studied previously by Wilkins and co-workers,[3] the method of analysis and the experimental conditions were different from those used in the present study.

Experimental Section

Materials. The concentrations of ca. 0.04 M $NiCl_2 \cdot 6H_2O$ (Fisher) stock solutions were determined by either atomic absorption or EDTA titration. Disodium adenosine 5′-triphosphate (Sigma) and 2,2′-bipyridine (Fisher) were used without further purification. All solutions were prepared with triply purified water containing 0.1 M KCl to maintain an approximately constant ionic strength. The stopped-flow solutions described below were prepared daily. A 0.001 M 2,2′-bipyridine stock solution was prepared weekly.

Equipment. The kinetic experiments were carried out on a Gibson-Durrum stopped-flow spectrometer thermostated at 15 °C. The concentration and pH range was also scanned by temperature-jump spectroscopy; no other effects were observed. A Corning digital potentiometer

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(14) Ni|ATP|bpy refers to the *system* containing nickel(II), ATP, and bipyridine as a whole. Ni(ATP)(bpy) refers to a specific complex.
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