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Pyrophosphate and ATP as Stabilizing Ligands for High-Valent Nickel Complexes

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ATP stabilizes trivalent nickel complexes which suggests that another plausible role of ATP in biological systems is the stabilization of high-valent transition metal complexes.

Anionic ligands, which are hard acids e.g. SO_4^{2-} or $CH_3CO_2^-$, are known to stabilize, through axial coordination, Ni^{III} complexes with tetraazamacrocyclic ligands, e.g. (cyclam)Ni^{III} (cyclam = 1,4,8,11-tetraazacyclotetradecane).[1–4] Thus, good stabilizing anionic ligands are needed in order to synthesize stable high-valent nickel complexes. It has been observed that phosphate[4] and its derivatives are good axial ligands and therefore the effect of $P_2O_7^{4-}$ as a ligand was studied. The electrochemical results (CV) of the oxidation of $Ni^{II}L^{2+}$ in the presence of pyrophosphate on a glassy carbon electrode (Figure 1) point out that pyrophosphate forms a very stable complex; the formation constant of the pyrophosphate complex $Ni^{III}L(P_2O_7)_2^{5-}$ at pH = 7.0 is calculated from the intercept of the line in the inset of Figure 1 (Nernst equation) to be $K_{eq} = 9.6{\cdot}10^{10}\ \text{M}^{-2}$ {the stability constants were calculated using the total concentration of pyrophosphate in the solution, relative to $E_{1/2}[NiL(H_2O)_2^{3+}/NiL^{2+}]$ at pH = 2.0[4b]}. One obtains $E_{1/2}$ = 0.44 V (vs. SCE), for the Ni$^{III/II}$L couple in solutions containing 0.016 M pyrophosphate (as pK_{a4} of $H_4P_2O_7$ is 8.66, it is reasonable to assume that at pH = 7.0, due to the inductive effect of the central Ni^{III} ion,[4] the ligand is $P_2O_7^{4-}$). The electrochemical results are independent of the presence of dioxygen in the solution. Furthermore, the cyclic voltammogram at pH = 3.0, consists of two pseudo-reversible oxidation waves (Figure 1). The first wave is the oxidation of divalent nickel to trivalent nickel (one-electron oxidation) and the second wave might be attributed to the oxidation of trivalent nickel to tetravalent nickel. In order to characterize the electrochemical oxidation product, preparative electrolysis at 640 mV (vs. SCE) was performed and the resulting oxidized complex was characterized by EPR. The results point out that it is indeed a trivalent nickel complex (the measured g values are typical for trivalent (cyclam)nickel: $g_\perp = 2.220$; $g_\parallel = 2.022$; $g_{av} = 2.154$, at 200 K).[5] In order to determine whether an Ni^{IV} complex is formed during the second oxidation wave, a second preparative electrolysis (vs. SCE) was performed by applying a controlled voltage of 800 mV to a solution containing $Ni^{III}L(P_2O_7)_2^{5-}$, and the resulting oxidized solution was characterized by EPR. However, formation of tetravalent (cyclam)nickel was not observed, probably due to the fast decomposition of the unstable Ni^{IV} complex. A similar result was obtained when a CV experiment was performed using the electrolyzed solution, beginning the cycle at +0.9 V. The electrochemical results were corroborated by pulse radiolysis experiments which show that $Ni^{IV}L(P_2O_7)_n^{4-4n}$ (n = 1 or 2) can be formed, but indeed is short-lived. The reaction of $Ni^{III}L(P_2O_7)_2^{5-}$ with the $N_3^{\cdot}$ radical, which is an outer-sphere oxidizing agent[6] with E^0 = 1.3 vs. NHE,[6] was studied by pulse radiolysis: $Ni^{III}L(P_2O_7)_2^{5-}$ was prepared by oxidation of $Ni^{II}L^{2+}$ with $Na_2S_2O_8$ at pH = 3.0[7] in a solution containing 0.016 M $Na_4P_2O_7$. To this solution 0.1 M NaN_3 was added, which did not affect the spectrum of the $Ni^{III}L(P_2O_7)_2^{5-}$ complex. Upon exposure to ionizing radiation, $N_3^{\cdot}$ radicals were formed accoding to Equations (1), (2) and (3) in less then 5 µs.

$$H_2O \xrightarrow{e^-,\ \gamma} {}^{\cdot}OH,\ H^{\cdot},\ e^-_{aq},\ H_2,\ H_2O_2,\ H_3O^+,\ OH^-$$
$$G({}^{\cdot}OH) = 2.65;\ G(H^{\cdot}) = 0.60;\ G(e^-_{aq}) = 2.65;\ G(H_2) = 0.45;\ G(H_2O_2) = 0.75^{[8]} \qquad (1)$$

$$e^-_{aq} + N_2O + H_2O \rightarrow {}^{\cdot}OH + OH^- + N_2;\ k = 9.1{\cdot}10^9\ \text{M}^{-1}\,\text{s}^{-1[9]} \qquad (2)$$

$${}^{\cdot}OH + N_3^- \rightarrow {}^{\cdot}N_3;\ k = 1.0{\cdot}10^{10}\ \text{M}^{-1}\,\text{s}^{-1[10]} \qquad (3)$$

The reaction of ${}^{\cdot}N_3$ with $Ni^{III}L(P_2O_7)_2^{5-}$ results in the formation of an intermediate with a strong absorption band shifted to the red (450 nm relative to that of Ni^{III}L-

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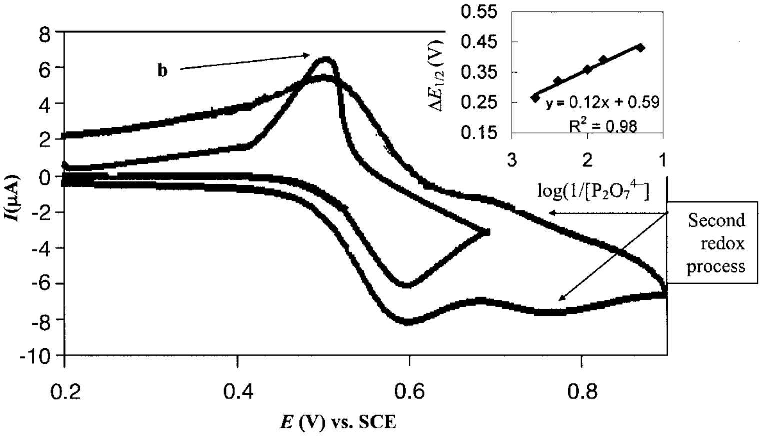

Figure 1. Electrochemical oxidations of $Ni^{II}L^{2+}$ in the presence of $Na_4P_2O_7$. Solution composition: 0.1 м $NaClO_4$, pH = 3.0, 0.001 м $Ni^{II}L^{2+}$, 0.016 м pyrophosphate, scan rate 50 mV/s; b: the same performed only for the 1st oxidation wave. Inset: Dependence of $\Delta E_{1/2}$ on log $(1/[P_2O_7^{4-}])$, where $\Delta E_{1/2}$ is the difference between $E_{1/2}$ for NiL^{2+} in the absence of $P_2O_7^{4-}$ and the measured $E_{1/2}$.

$(P_2O_7)_2^{5-}$ at 380 nm; Figure 2), which plausibly represents the $Ni^{IV}L$ complex. The kinetics of formation of the intermediate obey a pseudo-first-order rate law, i.e. the observed rate is proportional to $[Ni^{III}L(P_2O_7)_2^{5-}]$. The rate of the reaction is independent of (i) $[N_3^-]$, (ii) $[N_2O]$, (iii) pH in the range 6–11 and wavelength, and the rate constant is $k\{LNi^{III}(P_2O_7)_2^{5-} + N_3^{\cdot}\} = (3.1 \pm 0.4) \times 10^8\ M^{-1}\,s^{-1}$. Thus, it is suggested that the reaction observed occurs between the trivalent nickel complex and the azide radical to produce the tetravalent nickel complex according to Equation (4).

$$[LNi^{III}(P_2O_7)_2]^{5-} + N_3^{\cdot} \rightarrow [LNi^{IV}(P_2O_7)_2]^{4-} + N_3^- \quad (4)$$

The formation of the transient is followed by three time-separated processes which obey first-order rate laws. The first two are probably isomerisation processes, with rate constants of ca. $2 \cdot 10^3$ and 90 s^{-1} respectively; similar rates were reported for the isomerisation reactions of $Ni^{III}L$ complexes.[1] The third reaction is the decomposition of the tetravalent complex in which the absorption spectrum due to the transient disappears. The suggestion that the transient is $[LNi^{IV}(P_2O_7)_2]^{4-}$ is corroborated by its long life time (Figure 2). The rate of decomposition of the transient is ca. 0.25 s^{-1} and is nearly independent on pH, in the range 6 < pH < 10, complex concentration and the presence of dioxygen; all these properties point out that the transient formed is not a ligand-based radical.

As $P_2O_7^{4-}$ was found to stabilize the $Ni^{III}L$ complexes, it was decided to study the effect of ATP as a ligand, which might form the stable complex $Ni^{III}L(ATP)_2^{5-}$. It is indeed observed that ATP reacts with $Ni^{III}L(H_2O)_2^{3+}$ to form a stable $Ni^{III}L(ATP)_2^{5-}$ complex. From the electrochemical results (Figure 3), which point out that ATP forms a very stable complex, one calculates the formation constant of the ATP complex $Ni^{III}L(ATP)_2^{5-}$ to be $K_{eq} = 1.2 \cdot 10^{11}\ M^{-2}$ and $E_{1/2} = 0.41$ V (vs. SCE) for the $Ni^{III/II}L$ couple in solutions containing 0.016 м ATP (the stability constants were calculated using the total concentration of ATP in the solution). As expected, the electrochemical results also point out that the cathodic shift (compared to $Ni^{II}L$) at pH = 7.0 is higher than that at pH = 5.0 ($K_{eq} = 2.0 \cdot 10^8\ M^{-2}$ and $E_{1/2} = 0.51$ V

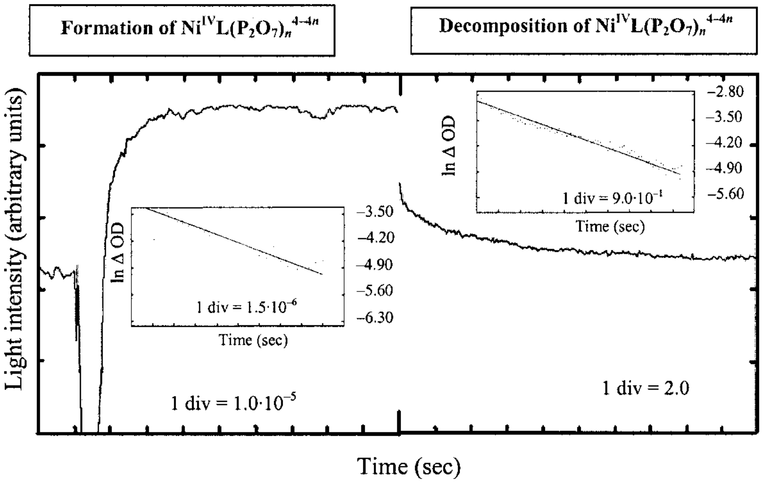

Figure 2. Pulse radiolysis of $Ni^{III}L^{2+}$ in the presence of $Na_4P_2O_7$. Solution composition: $4 \cdot 10^{-4}$ м $Ni^{III}L(SO_4)_2^-$, 0.1 м pyrophosphate, 0.02 м NaN_3, pH = 8.0; λ_{max} = 450 nm.

for the $Ni^{III/II}L$ couple in solutions containing 0.016 M ATP at pH = 5.0). This pH effect is attributed to the pK_a values of ATP ($pK_{a1} = 1.77$; $pK_{a2} = 3.96$; $pK_{a3} = 6.24$).[11] Preparative electrolysis of a solution containing $Ni^{II}L$ in the presence of ATP at 420 mV (vs. SCE) yields an $Ni^{III}L(ATP)_2^{5-}$ complex which is stable for hours in Ar- or air-saturated solutions (as in the $P_2O_7^{4-}$ system it is assumed that due to the inductive effect of the central Ni^{III} ion the ligand is ATP^{4-}). The EPR spectrum at 200 K ($g_\perp = 2.209$; $g_\parallel = 2.025$; $g_{av} = 2.148$, 200 K) is in agreement with this assignment. However, the electrochemical oxidation of $Ni^{II}L^{2+}$ in aerated solutions containing ATP is an irreversible process (Figure 3). This observation suggests that the $Ni^{III}L(ATP)_2^{5-}$ complex formed is synergistically oxidized by the electrode and by O_2 causing a decomposition of the complex. The results demonstrate that pyrophosphate and ATP stabilize high-valent transition metal complexes. Thus, it is reasonable to suggest that another role of ATP in biological systems is the stabilization of high-valent transition metal complexes, e.g. Fe^{III} and Mn^{III}.

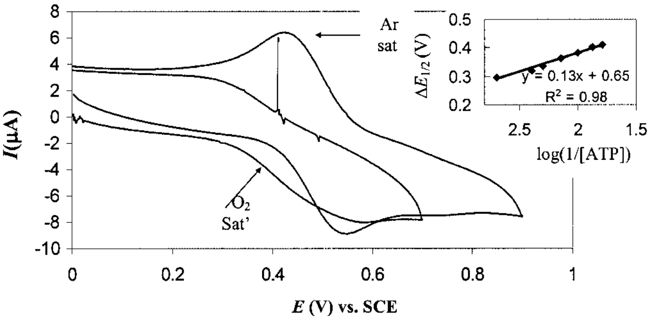

Figure 3. Electrochemistry of $Ni^{II}L^{2+}$ in the presence of ATP. Solution composition: 0.1 M $NaClO_4$, pH = 6.0; a: Ar-saturated; 0.01 M ATP, 0.001 M $Ni^{II}L^{2+}$; b: O_2-saturated; 0.01 M ATP, 0.001 M $Ni^{II}L^{2+}$; scan rate 50 mV/s. Inset: Dependence of $\Delta E_{1/2}$ on log (1/[ATP]), where $\Delta E_{1/2}$ is the difference between $E_{1/2}$ for NiL^{2+} in the absence of ATP and the measured $E_{1/2}$.

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