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5,7,7,12,14,14-Hexamethyl-1,4,8,11-tetraazacyclotetradecane-nickel(II) as a catalyst for oxidations by superoxide in aqueous solutions. A pulse radiolysis study

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Abstract

The title complex, NiL^{2+} is oxidized in aqueous solutions in the pH range 3–7 in the presence of stabilizing anions X ($X = HCO_2^-$, SO_4^{2-} and PO_4^{3-}), by $HO_2^{\bullet}$ free radicals to $Ni(III)LX_2$. The latter complexes are powerful oxidizing agents which oxidize HCO_2^-, $S_2O_3^{2-}$, NO_2^- and ascorbate. Thus the title complex acts as a catalyst for oxidations by the superoxide free radical which is in equilibrium with the $HO_2^{\bullet}$ free radical. The results point out that in the presence of appropriate transition metal complexes the superoxide free radical is a potent oxidizing agent and suggest that this might cause some of the aspects of its toxicity.

The superoxide free radical has been suggested to have a key role in many deleterious biological processes [1]. It is commonly believed [2] that the toxicity of the superoxide is due to its reduction potential, $E^0(O_2/O_2^-) = -0.16$ V versus NHE at 1 atm. O_2 [3]. The argument favoring this explanation of the mechanism of toxicity stems from the general accepted notion that superoxide is a poor oxidant in aqueous solutions [4], though thermodynamically it has a redox potential of $E^0(O_2^-/H_2O_2) = 0.87$ V versus NHE at pH 7 [5]. The kinetic barrier to oxidations by superoxide is that the primary products of oxidation via the outer sphere mechanism O_2^{2-} and even by hydrogen abstraction HO_2^- are unstable in neutral aqueous solutions, due to the high pK_a of H_2O_2 [6]. However if the products of reaction are initially stabilized by complexation to a metal cation oxidation by superoxide should be conceivable. Therefore it is plausible that the toxicity of superoxide might be due, at least in some systems to its oxidizing properties [7]. Indeed it was shown that superoxide oxidizes $Mn(II)nta_{aq}$ [8], $Mn(II)edta_{aq}$ [8], $Co(II)nta_{aq}$ [8] and $Mn(II)(P_4O_7)_{aq}$ [9], in neutral aqueous solutions. The reported mechanism of reaction being [8]

$$M(II)L + O_2^- \xrightarrow{\text{fast}} LM(III)(O_2^{2-}) \xrightarrow{\text{slow}} M(III)L + H_2O_2 \qquad (1)$$

The intermediate complexes $LM(III)O_2^{2-}$ were shown to oxidize several substrates of biological interest [9, 10].

Recently we have shown [11] that the $\cdot O_2CH_3$ radical oxidizes the complex, 1,4,8,11-tetraazacyclotetradecane-nickel(II), NiL'^{2+}, to the tervalent complex via

$$NiL'^{2+} + \cdot O_2CH_3 \longrightarrow L'Ni^{III}\text{–}O_2CH_3^{2+} \qquad (2)$$

The product complex is a powerful oxidizing agent. It seemed therefore of interest to study whether HO_2, or even O_2^-, might oxidize analogous nickel complexes. For the present study we have chosen the complex 5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane-nickel(II), NiL^{2+}, as $E^0(NiL^{3+}/NiL^{2+}) > E^0(NiL'^{3+}/NiL'^{2+})$ [12].

Air or oxygen saturated solutions containing $1\text{–}10 \times 10^{-4}$ M $NiL(ClO_4)_2$, 5×10^{-3} M HCO_2Na and 0.01–1 M NaX (where $X = HCO_2^-$, SO_4^{2-} and PO_4^{3-}) in the pH range 3.0–7.0 were irradiated by a short pulse of 5 MeV electrons from the linear accelerator at the Hebrew University of Jerusalem. The experimental setup and procedures were identical to those described earlier in detail [13].

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Under these conditions all the primary free radicals are transformed into a mixture of O_2^- and HO_2, the composition of which depends on pH, via the following reactions

$$e_{aq}^- + O_2 \longrightarrow \cdot O_2^- \tag{3}$$

$k = 1.9 \times 10^{10}\ M^{-1}s^{-1}$ [14]

$$\cdot O_2^- + H_3O^+ \rightleftharpoons HO_2 \tag{4}$$

$pK_a = 4.8$ [15]

$$\cdot OH/H + HCO_2^- \longrightarrow \cdot CO_2^- + H_2O/H_2 \tag{5}$$

$k_{OH} = 2.9 \times 10^9\ M^{-1}\ s^{-1}$ [14], $k_H = 1.3 \times 10^8\ M^{-1}\ s^{-1}$ [14]

$$\cdot CO_2^- + O_2 \longrightarrow \cdot O_2^- \tag{6}$$

$k = 4.2 \times 10^9\ M^{-1}\ s^{-1}$ [16]

When the ratio of $[NiL^{2+}]/[O_2]$ is high O_2^- is also formed via

$$NiL^{2+} + e_{aq}^- \longrightarrow NiL^+ \tag{7}$$

$k = 5.6 \times 10^{10}\ M^{-1}\ s^{-1}$ [17]

$$NiL^{2+} + \cdot CO_2^- \longrightarrow NiL^+ + CO_2 \tag{8}$$

$k = 5.7 \times 10^9\ M^{-1}\ s^{-1}$ [17]

$$NiL^+ + O_2 \longrightarrow NiL^{2+} + O_2^- \tag{9}$$

$k = 1.6 \times 10^9\ M^{-1}\ s^{-1}$ [17]

When the ratio $[NiL^{2+}]/[HCO_2^-]$ is high some $Ni(III)LX_2$ is formed via

$$NiL^{2+} + \cdot OH \longrightarrow NiL^{3+} \tag{10}$$

$k = 1.5 \times 10^9\ M^{-1}\ s^{-1}$ [18]

$$NiL^{3+} + 2X \longrightarrow Ni(III)LX_2 \tag{11}$$

Under these conditions a process obeying a first order rate law and producing a stable product, i.e. $t_{1/2} > 2$ min, is observed. The rate of this process depends linearly on $[NiL^{2+}]$, Fig. 1, but also on [X] and pH. The spectra of the products, Fig. 2, are identical to those of $Ni(III)LX_2$ formed in identical solutions but N_2O saturated. In the latter solutions reaction (9) is replaced by

$$NiL^+ + N_2O \xrightarrow{H_2O} NiL^{3+} + N_2 + 2OH^- \tag{12}$$

$k = 3.9 \times 10^7\ M^{-1}\ s^{-1}$ [17]

followed by reaction (11) [19]. It is therefore suggested that the process observed in slightly acidic air or oxygen saturated solutions is

$$NiL^{2+} + HO_2 + X \longrightarrow LNi(III)(O_2H)X \tag{13}$$

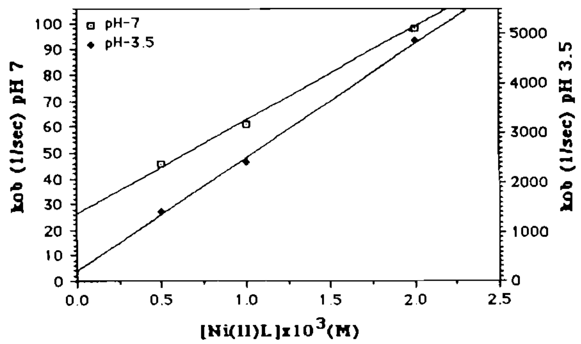

Fig. 1. Dependence of the observed rate of the formation of $Ni(III)LX_2$ on [NiL(II)] in air saturated solutions at pH 3.5 and pH 7.0. Solution composition: $[HCO_2Na] = 5 \times 10^{-3}$ M, $[NaH_2PO_4] = 0.1$ M.

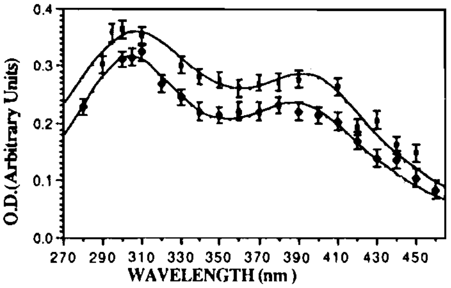

Fig. 2. UV–Vis spectra of pulse radiolytically generated $LNi(III)X_2$. Solution composition: 1×10^{-4} M $Ni(II)L(ClO_4)$, 0.1 M HCO_2Na at pH 4.0. Upper spectrum: N_2O saturated solutions, i.e. the product is formed via reactions (13) and (14). Lower spectrum: Air saturated solutions, i.e. the product is formed via reactions (12) and (11).

followed by

$$LNi(III)(O_2H)X + X + H_3O^+ \longrightarrow LNi(III)X_2 + H_2O_2 \tag{14}$$

where reaction (13) is the rate determining step. (The intercepts in Fig. 1 are due to the contribution of the disproportionation reaction of the free radicals.) We have not observed in any of the experiments, though we have looked for it, a spectrum which can be attributed to $LNi(III)(O_2H)X$. It is expected that the spectrum of $LNi(III)(O_2H)X$ will be shifted considerably to the red relative to that of $LNi(III)X_2$ as the optical electronegativity of HO_2^- is much smaller than that of the Xs used in this study. Furthermore the kinetics of oxidation of different substrates by $LNi(III)X_2$, see below, are identical whether they are formed via reactions (13) and (14) or (12) and (11).

The dependence of the rate of reaction (13) on [X] indicates that X is bound to the nickel coherently with the reaction with HO_2. This seems to stem from the effect of the ligation of X to NiL^{3+} on its redox potential [18]. The specific rates calculated for reaction (13) where $X=H_2PO_4^-$ or HPO_4^{2-} at pH 3.5 and pH 7.0 are 2.3×10^6 and 3.5×10^4 M^{-1} s^{-1}, respectively (Fig. 1). The ratio between these rates (66) is somewhat smaller than the expected ratio of 315 calculated, using the pK_a of HO_2 and assuming that O_2^- does not react with NiL^{2+}. However as the nature of X is different at the two pHs we suggest that even at pH 7.0 we probably observe only oxidations by HO_2.

The product complexes $LNi(III)X_2$ oxidize HCO_2^- to CO_2, $S_2O_3^{2-}$, NO_2^- and ascorbate. The mechanism and the kinetics of these reactions depend in a complex way on the nature of X and its concentration; these mechanisms are presently being studied in detail. The specific rate of the oxidation of ascorbate by $LNi(III)X_2$, where $X=HPO_4^{2-}$ (0.02 M), at pH 7.0 is 2×10^5 M^{-1} s^{-1}.

The major conclusion from these experiments is that HO_2 can oxidize transition metal complexes even in neutral aqueous solutions producing powerful oxidizing agents. The redox potential for $LNi(III)(H_2PO_4)^-/NiL^{2+}$ in 0.3 M $H_2PO_4^-$ at pH 2 is 0.96 V [19] and for $LNi(III)SO_4^{2-}/NiL^{2+}$ in 0.5 M SO_4^{2-} is 0.88 V versus NHE [19]. Furthermore these complexes are in equilibrium with $LNi(III)H_2OX$, NiL^{3+} and $LNiOH^{2+}$ which are considerably stronger oxidizing agents [20]. Thus the results suggest that the toxicity of superoxide might indeed stem from its oxidizing properties.

Finally it should be pointed out that the nickel complex acts in these experiments as a catalyst for the oxidation of HCO_2^-, $S_2O_3^{2-}$, NO_2^- and ascorbate.

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