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Mechanism of Oxidation of (*meso*-5,7,7,12,14,14-Hexamethyl-1,4,8,11-tetraazacyclotetradecane)nickel(II) by HO_2 Free Radicals in Aqueous Solutions. A Pulse Radiolysis Study

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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 $H_2PO_4^-$, by $HO_2^\bullet$ free radicals to $Ni^{III}LX_2$. The dependence of the rate of formation on $[NiL^{2+}]$ and X indicates that the $HO_2^\bullet$ radical reacts with a $[NiL^{2+}]$ complex in the ion pair $[NiL^{2+},X]$, forming the final products. The volumes of activation of the oxidation processes were measured; an analysis of the data indicates that the ion pairs involved are contact ion pairs. The results indicate 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.

Introduction

The involvement of $O_2^{\bullet-}$ in biological processes has been recognized since the discovery of superoxide dismutase (SOD) in 1969.[2] The superoxide radical is produced during normal metabolism of aerobic organisms, and some of the dioxygen is converted to $O_2^{\bullet-}$ during the aerobic respiration.[3] The superoxide radical is also generated by the oxidation of xanthine by xanthine oxidase,[2,4] and is produced during the autooxidation of several biological compounds, e.g., hemoglobin, flavines, epinephrine, etc.

The rate of reaction of the disproportionation reaction

$$2O_2^{\bullet-} + 2H^+ \rightarrow O_2 + H_2O_2 \qquad (1)$$

depends on the pH; at physiological pH the rate constant of the reaction is 5×10^5 M^{-1} s^{-1}.[5] The SOD enzyme catalyzes the disproportionation of $O_2^{\bullet-}$ at physiological pH with a rate constant of (2–3) $\times 10^9$ M^{-1} s^{-1}.[6] As the sole function of this enzyme found till now is to catalyze this reaction, it was suggested that the superoxide radical is toxic, and must be removed rapidly from the cells. Indeed in the literature the superoxide free radical has been suggested to have a key role in numerous deleterious biological processes.[7]

Chemical and physiological studies suggest that $O_2^{\bullet-}$ is not very reactive toward amino acids, fatty acids, DNA, etc.,[8] and one cannot explain the toxicity of $O_2^{\bullet-}$ by its direct reaction with these biomolecules without the participation of another entity, though it was shown that $O_2^{\bullet-}$ does react with a number of small molecules such as epinephrine, bilirubin, etc.[8]

To explain the toxicity of superoxide, a mechanism involving indirect deleterious activity of the superoxide radical has been suggested. According to this mechanism, $O_2^{\bullet-}$ serves as a precursor to a highly toxic entity, the $^\bullet OH$ radical. The reaction that was suggested for this process is the Haber–Weiss reaction:[9]

$$O_2^{\bullet-} + H_2O_2 \rightarrow O_2 + OH^- + {}^\bullet OH \qquad (2)$$

The Haber–Weiss reaction is allowed thermodynamically, but kinetically the rate of reaction 2 is very slow;[10] therefore, the toxicity of superoxide cannot be explained by the formation of $^\bullet OH$ radicals via reaction 2 as $O_2^{\bullet-}$ disproportionates much faster through reaction 1 and even faster in the presence of the SOD enzyme.

However, the "Haber–Weiss" reaction is catalyzed by transition-metal complexes; i.e.[11,12]

$$O_2^{\bullet-} + LM^{n+} \rightarrow O_2 + LM^{(n-1)+} \qquad (3)$$

$$LM^{(n-1)+} + H_2O_2 \rightarrow LM^{n+} + OH^- + {}^\bullet OH \qquad (4)$$

According to this mechanism, the toxicity of $O_2^{\bullet-}$ is due to two consecutive steps. The first reaction involves the reduction of a transition-metal complex (reaction 3), and the second step is the reaction of the reduced complex with H_2O_2 in a "Fenton-like" reaction (reaction 4) to produce $^\bullet OH$ radicals as the deleterious entity. According to this mechanism, the toxicity of $O_2^{\bullet-}$ is due to its reducing properties.

Since in vivo the superoxide is neither one of the most abundant reducing agents nor one of the strongest reducing agents that are present in the cell,[13] it is rather puzzling how we survive in the reducing environment of the cells, as some of the biological reductants can easily replace $O_2^{\bullet-}$ in reducing transition-metal complexes. Therefore recently, an alternative mechanism to explain the toxicity of $O_2^{\bullet-}$ was proposed.[14] According to this hypothesis, $O_2^{\bullet-}$ acts as an oxidizing agent, rather than as a reducing one:

$$LM^{n+} + O_2^{\bullet-} + 2H^+ \rightarrow LM^{(n+1)+} + H_2O_2 \qquad (5)$$

or

$$LM^{n+} + O_2^{\bullet-} \rightarrow LM^{(n+1)}O_2^{2-} \qquad (6)$$

According to this hypothesis, the superoxide radical acts as the precursor of a high-valent transition-metal complex, e.g., Cu(III), Fe(IV), and Mn(III), etc., and the damage occurs via reaction of this complex with the target. It is a generally accepted notion that the superoxide is a poor oxidant in aqueous solutions,[15] though thermodynamically it has a redox potential of $E°(O_2^{\bullet-}/H_2O_2)$ = 0.87 V vs NHE at pH 7.[16] 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.[17] However, if the products of reaction are initially

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(2) McCord, J. M.; Fridovich, I. *J. Biol. Chem.* **1969**, *244*, 6049.

(3) (a) Boveris, A. *Adv. Exp. Med. J. Biol.* **1977**, *78*, 67. (b) Fridovich, I. *Photochem. Photobiol.* **1978**, *28*, 733.

(4) McCord, J. M.; Fridovich, I. *J. Biol. Chem.* **1969**, *243*, 5753.

(5) Behar, D.; Czapski, G.; Rabani, J.; Dorfman, L. M. *J. Phys. Chem.* **1970**, *74*, 3209.

(6) Fielden, E. M.; Robert, P. B. *Biochem. J.* **1974**, *139*, 49.

(7) (a) Fridovich, I. *Acc. Chem. Res.* **1974**, *5*, 321. (b) See for example, Harman, D. Free Radicals, Aging and Degenerative Diseases In *Modern Aging Research*; Johnson, J. E., Jr., Walford, R., Harman, D., Miquel, J., Eds.; Alan R. Liss, Inc.: New York, 1986; Vol. 8, p 3. (c) Cross, C. E. *Ann. Intern. Med.* **1987**, *107*, 526. (d) Byczkowski, J. Z.; Gessner, T. *Int. J. Biochem.* **1988**, *20*, 569.

(8) Bielski, B. H. J.; Cabelli, D. E.; Arudi, R. L.; Ross, A. B. *J. Phys. Chem. Ref. Data* **1985**, *14*, 1101.

(9) Haber, F.; Weiss, J. *Proc. R. Soc. London, A* **1934**, *47*, 332.

(10) Czapski, G.; Ilan, Y. *Photochem. Photobiol.* **1978**, *28*, 651.

(11) Fenton, H. J. H. *J. Chem. Soc.* **1894**, *65*, 899.

(12) Walling, C. *Acc. Chem. Res.* **1975**, *8*, 125.

(13) (a) White, A.; Handler, P.; Smith, E. L. *Principles of Biochemistry*; McGraw-Hill: New York, 1973. (b) Foyer, C. H.; Halliwell, B. *Planta* **1976**, *122*, 21. (c) Tozum, S. R.; Gallon, J. R. *Gen. Microbiol.* **1979**, *11*, 313.

(14) Czapski, G.; Goldstein, E.; Meyerstein, D. *Free Radical Res. Commun.* **1988**, *4*, 231.

(15) Bielski, B. H. J.; Gibichik, J. M. *Adv. Radiat. Chem.* **1970**, *2*, 177.

(16) Fee, J. A.; Valentine, J. S. In *Superoxide and Superoxide Dismutases*; Michelson, A. M., McCord, J. M., Fridovich, I., Eds.; Academic Press: London, 1977; p 26.

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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.[16] Indeed, it was shown that superoxide oxidizes $Mn^{II}nta_{aq}$,[18] $Mn^{II}edta_{aq}$,[18] $Co^{II}nta_{aq}$,[18] and $Mn^{II}(P_4O_7)_{aq}$[19] in neutral solutions, the reported mechanism of the reaction being[18]

$$M^{II}L + O_2^{\bullet -} \xrightarrow{\text{fast}} LM^{III}(O_2^{2-}) \xrightarrow[{[H^+]}]{\text{slow}} M^{III}L + H_2O_2 \tag{7}$$

The intermediate complexes were shown to oxidize several substrates of biological interest.[19,20] However, all these complexes have rather low oxidation potentials, and therefore their oxidized forms are not expected to be capable of causing biologically deleterious processes. Recently, we have shown[21] that the $^{\bullet}O_2CH_3$ radical oxidizes the complex 1,4,8,11-tetraazacyclotetradecane–nickel(II), NiL'^{2+}, to the tervalent complex via

$$NiL'^{2+} + {}^{\bullet}O_2CH_3 \rightarrow L'NiO_2CH_3^{2+} \tag{8}$$

The product complex is a powerful oxidizing agent. It seemed therefore of interest to study whether $HO_2^{\bullet}$, or even $O_2^{\bullet -}$, might oxidize analogous nickel complexes. For the present study we have chosen the complex (*meso*-5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane)nickel(II), NiL^{2+}, as $E°(NiL^{3+}/NiL^{2+}) > E°(NiL'^{3+}/NiL'^{2+})$[22] as evidence of its oxidation would prove that indeed the superoxide radical is capable of producing rather powerful transition metal oxidizing agents in aqueous solutions.

Experimental Section

Materials. All solutions were prepared from A.R. grade chemicals and from distilled water further purified by passing through a Milli Q Millipore setup, final resistivity ≥10 MΩ/cm. $Ni^{II}L(ClO_4)_2$ was prepared according to literature methods.[23]

N_2O was first bubbled through two scrubbing bottles containing VSO_4 in dilute H_2SO_4 over Zn amalgam, followed by two scrubbing bottles containing distilled water for removing traces of oxygen before saturating the sample understudy.

Air-, oxygen-, or N_2O-saturated solutions containing $(1–10) \times 10^{-4}$ 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 $H_2PO_4^-$) in the pH range 3.0–7.0 were used.

Techniques. Solutions were handled by syringe techniques. Pulse radiolysis experiments were carried out at the Varian 7715 linear electron accelerator facility of the Hebrew University of Jerusalem; 0.5–1.5-μs, 5-MeV, and 200-mA pulses were used. The dose per pulse was in the range of 1000–3000 rad/pulse. The irradiations were done in a 4-cm Spectrosil cell with an optical path length of 12.1 cm. A 150-W Xe–Hg lamp was used as the analytical light source. The detection system included a Bausch & Lomb grating monochromator, model D330/D331 MK II, and a IP28 photomultiplier. The signal was transferred through a Sony/Tektronix 390AD programmable digitizer to a micro PDP-11/24 computer, which operated the whole pulse radiolysis system and the processing of the results.

High-Pressure Experiments. The high-pressure setup was identical with that described elsewhere in detail.[24] The window of the high-pressure cell through which the radiation penetrates the cell was however replaced by a 5-mm sapphire window. The internal pillbox was placed as near as possible to the window so that the high-energy electrons would have a minimal path through the surrounding water medium.

Results and Discussion

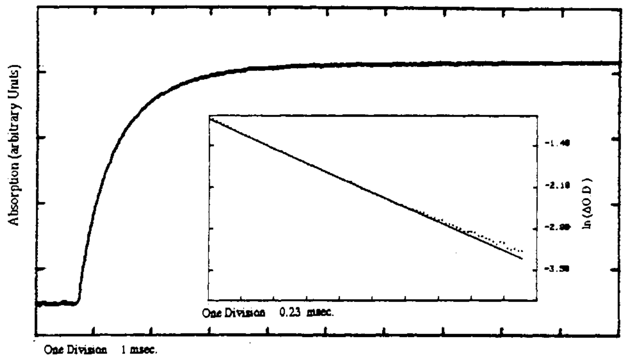

Figure 1. Computer output of the time dependence of the light absorption (320 nm) of the sample following the pulse. Solution composition: 0.1 M sulfate, 5×10^{-3} M HCO_2Na, 1×10^{-4} M $Ni^{II}L(ClO_4)_2$, pH 3.4 ± 0.1, air-saturated. Inset: fit of the formation to the first-order rate law.

Air- or oxygen-saturated solutions containing $(1–10) \times 10^{-4}$ 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 $H_2PO_4^-$) in the pH range 3.0–7.0 were irradiated by a short pulse from the linear accelerator. Under these conditions all the primary free radicals are transformed within less than 10 μs into a mixture of $O_2^{\bullet -}$ and $HO_2^{\bullet}$, the composition of which depends on pH, via the following reactions:

$$e^-_{aq} + O_2 \rightarrow O_2^{\bullet -} \tag{9}$$

$k = 1.9 \times 10^{10}\ M^{-1}\ s^{-1}$[25]

$$O_2^{\bullet -} + H_3O^+ \rightarrow HO_2^{\bullet} \tag{10}$$

$pK_a = 4.8$[26]

$$^{\bullet}OH/H^{\bullet} + HCO_2^- \rightarrow {}^{\bullet}CO_2^- + H_2O/H_2 \tag{11}$$

$k_{OH} = 2.9 \times 10^9\ M^{-1}\ s^{-1}$[25] $k_H = 1.3 \times 10^8\ M^{-1}\ s^{-1}$[25]

$$^{\bullet}CO_2^- + O_2 \rightarrow O_2^{\bullet -} + CO_2 \tag{12}$$

$k = 4.2 \times 10^9\ M^{-1}\ s^{-1}$[27]

When the ratio of $[NiL^{2+}]/[O_2]$ is high, a condition which is correct only for some of the solutions used, $O_2^{\bullet -}$ is also formed via

$$NiL^{2+} + e^-_{aq} \rightarrow NiL^+ \tag{13}$$

$k = 5.6 \times 10^{10}\ M^{-1}\ s^{-1}$[28]

$$NiL^{2+} + {}^{\bullet}CO_2^- \rightarrow NiL^+ + CO_2 \tag{14}$$

$k = 5.7 \times 10^9\ M^{-1}\ s^{-1}$[28]

$$NiL^+ + O_2 \rightarrow NiL^{2+} + O_2^{\bullet -} \tag{15}$$

$k = 1.6 \times 10^9\ M^{-1}\ s^{-1}$[28]

When the ratio of $[NiL^{2+}]/[HCO_2^-]$ is high, $Ni^{III}LX_2$ is also formed via

$$NiL^{2+} + {}^{\bullet}OH \rightarrow NiL^{3+} \tag{16}$$

$k = 1.5 \times 10^9\ M^{-1}\ s^{-1}$[29]

$$NiL^{3+} + 2X \rightarrow Ni^{III}LX_2 \tag{17}$$

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, Figure 1. The spectra of the products formed in this process are identical to those of $Ni^{III}LX_2$ formed in identical solutions but

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(17) Cotton, F. A.; Wilkinson, G. In *Advanced Inorganic Chemistry*, 4th. ed.; J. Wiley & Sons: New York, 1980; p 496.

(18) Lati, I.; Meyerstein, D. *J. Chem. Soc., Dalton Trans.* **1978**, 1105.

(19) Cabelli, D. E.; Bielski, B. H. J. *J. Phys. Chem.* **1984**, *88*, 3111.

(20) Bielski, B. H. J.; Chan, P. C. *J. Am. Chem. Soc.* **1979**, *100*, 1920.

(21) Sauer, A.; Cohen, H.; Meyerstein, D. *Inorg. Chem.* **1988**, *27*, 4578.

(22) (a) Zeigerson, E.; Ginzburg, G.; Kirschenbaum, L. J.; Meyerstein, D. *Electroanal. Chem. Interfacial Electrochem.* **1981**, *127*, 113. (b) Zeigerson, E.; Bar, I.; Bernstein, J.; Kirschenbaum, L. J.; Meyerstein, D. *Inorg. Chem.* **1982**, *21*, 73.

(23) Tait, A. M.; Busch, D. H. *Inorg. Nucl. Chem. Lett.* **1972**, *8*, 491.

(24) (a) Van Eldik, R., Jonas, J., Eds. *High Pressure Chemistry and Biochemistry*; Reidel: Dordrecht, Holland, 1987. (b) Val Eldik, R. *Inorganic High Pressure Chemistry: Kinetics and Mechanisms*; Elsevier: Amsterdam, Holland, 1986.

(25) Buxton, G. V.; Greenstock, C. L.; Helman, W. P.; Ross, A. B. *J. Phys. Chem. Ref. Data* **1988**, *17*, 513.

(26) Bielski, B. H. J. *Photochem. Photobiol.* **1978**, *28*, 645.

(27) Ilan, Y. A.; Rabani, J. *Int. Radiat. Phys. Chem.* **1976**, *8*, 609.

(28) Jubran, N.; Ginzburg, G.; Cohen, H.; Koresh, Y.; Meyerstein, D. *Inorg. Chem.* **1985**, *24*, 251.

(29) Cohen, H.; Kirschenbaum, L. J.; Zeigerson, E.; Jaacobi, M.; Fuchs, E.; Ginzburg, G.; Meyerstein, D. *Inorg. Chem.* **1979**, *18*, 2763.

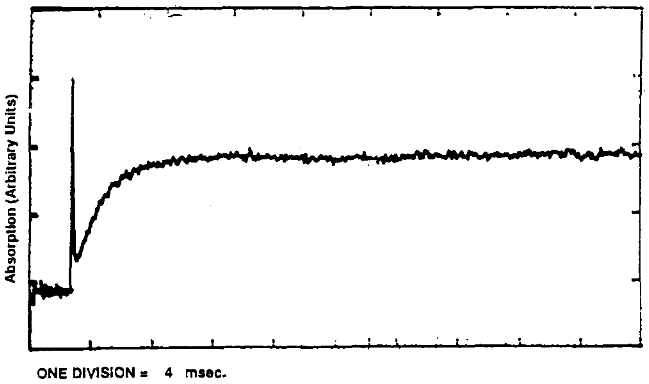

Figure 2. Computer output of the time dependence of the light absorption (300 nm) of the sample following the pulse. Solution composition: 0.1 M HCO_2Na, 1×10^{-4} M $Ni^{II}L(ClO_4)_2$, pH 4.0 ± 0.1, He-saturated with traces of O_2, ca. 2×10^{-5} M.

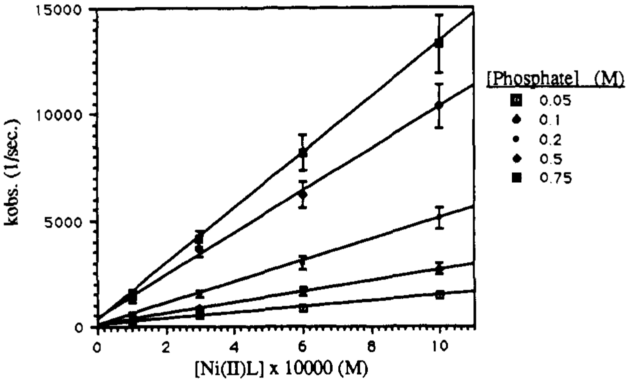

Figure 3. Dependence of the observed rate of formation of $Ni^{III}LX_2$ on $[Ni^{II}L(ClO_4)_2]$ in air-saturated solutions at pH 3.5 ± 0.1. Solution composition: $[HCO_2Na] = 5 \times 10^{-3}$ M, $[NaH_2PO_4]$ = 0.05, 0.1, 0.2, 0.5, 0.75 M.

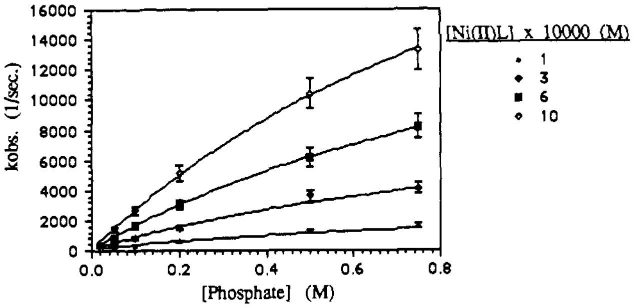

Figure 4. Dependence of the observed rate of formation of $Ni^{III}LX_2$ on $[NaH_2PO_4]$ in air-saturated solutions at pH 3.5 ± 0.1. Solution composition: $[HCO_2Na] = 5 \times 10^{-3}$ M, $[Ni^{II}L(ClO_4)_2] = 1 \times 10^{-4}$, 3×10^{-4}, 6×10^{-4}, 1×10^{-3} M.

N_2O-saturated and with no O_2 present.[30] In the latter solutions reaction 15 is replaced by

$$NiL^{+} + N_2O \rightarrow NiL^{3+} + N_2 + 2OH^{-} \qquad (18)$$

$$k = 3.9 \times 10^{7}\ M^{-1}\ s^{-1}\ {}^{28}$$

followed by reaction 17.[29] Furthermore, the kinetics of oxidation of different substrates by $LNi^{III}X_2$ are identical whether they are formed via reactions 18 and 17 or by the mechanism under study.[30] It is therefore suggested that the product formed in the observed process, in the presence of the three axial ligands HCO_2^-, SO_4^{2-}, and $H_2PO_4^-$, is $LNi^{III}X_2$. The rate of the formation of the product depends linearly on $[NiL^{2+}]$; the rate depends also on [X] but in a different way for each axial ligand and on the pH. The observed rates are independent of $[O_2]$. The detailed mechanism of this process is analyzed in detail below.

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 X's used in the study. It is therefore to be concluded that reaction 21 is considerably faster than reaction 20 under the experimental conditions. (The volumes of activation of reaction 20, see below, indicate that it proceeds via the inner-sphere mechanism. This conclusion is not surprising in view of the kinetic barriers to outer-sphere oxidations by $RO_2^{\bullet}$ free radicals.)

The yield of $Ni^{III}LX_2$ depends on [X]. No product is obtained, also not $Ni^{III}L_{aq}$, when [X] = 0. This observation is probably due to the stabilization of the tervalent nickel complex by the axial ligands.[22] Indeed $E^{\circ}(NiL^{2+}/NiL(H_2O)_2^{3+})$ is higher than the oxidation potential of $O_2^{\bullet-}$.[22]

When solutions containing a low concentration of dioxygen are irradiated, reactions 13–15 take place. Under these conditions the formation of NiL^+ via reactions 13 and 14 is observed. The spectrum of the first intermediate observed is indeed identical with that reported for NiL^+.[28] This intermediate disappears in a first-order reaction, the rate of which is proportional to $[O_2]$. The calculated rate of this process, $(1.5 \pm 0.5) \times 10^{9}\ M^{-1}\ s^{-1}$, is in accord with the reported rate of reaction 15.[28] At the end of this process nearly no absorption remains, again in accord with earlier observations.[28] Similar results were earlier[28] tentatively interpreted as indicating that reaction 15 occurs, but as neither $O_2^{\bullet-}$ nor $HO_2^{\bullet}$ was observed nor $Ni^{III}L$ formation observed, this assumption could not be proven. Under the present experimental conditions, i.e., in the presence high concentrations of X, one expects that the $O_2^{\bullet-}/HO_2^{\bullet}$ mixture, if formed, will form $Ni^{III}LX_2$ via reactions 19–21. This is indeed observed, Figure 2. In the figure the spike of absorption immediately after the pulse is due to NiL^+ as evidenced by its spectrum and rate of disappearance; the latter process is followed by the formation of $NiL(HCO_2)_2^-$ as in Figure 1. The rate of the last process in Figure 2 is in accord with the kinetic data obtained under conditions where the mixture $O_2^{\bullet-}/HO_2^{\bullet}$ is formed via reactions 9 and 12, and the spectra of the final products are those of $Ni^{III}LX_2$.

The apparent specific rates of the formation of $Ni^{III}LX_2$ via the process under study were calculated from measurements at two different pH's in air-saturated solutions containing a constant concentration of 0.1 M phosphate and 5×10^{-3} M HCO_2Na. The apparent specific rates at pH 3.5 and 7.0, respectively, are 2.3×10^{6} and $3.5 \times 10^{4}\ M^{-1}\ s^{-1}$. The ratio between these rates, 66, is somewhat smaller than the expected ratio of 315 calculated using the pK_a of $HO_2^{\bullet}$ and assuming that $O_2^{\bullet-}$ does not react with NiL^{2+}. However, as the nature of X is different at the two pH's, we suggest that even at pH 7.0 we probably observe only oxidations by $HO_2^{\bullet}$. (It is difficult to measure the rate in the pH range 4–6.5 due to the high value of k_1 in this pH range.[8])

Phosphate and Formate as Axial Ligands. Air- or oxygen-saturated solutions containing $(1-10) \times 10^{-4}$ M $NiL(ClO_4)_2$, 5×10^{-3} M HCO_2Na, and 0.01-1 M NaX (where X = $H_2PO_4^-$ and $HCOO^-$) at pH 3.5 were irradiated, and the formation of $Ni^{III}LX_2$ was observed.

We followed the rate of formation of the complexes, which have strong absorption bands at 400 nm in the phosphate-containing system and at 395 nm in the formate-containing system. A process obeying a first-order rate law was observed; this process is pseudo-first-order in $Ni^{II}L$, Figures 3 and 5 (Figure 5 is available as supplementary material). The dependence of the rate on the concentration of phosphate and formate is plotted in Figures 4 and 6 (Figure 6 is available as supplementary material). The fact that the rate increases with [X] up to a limiting value suggests that the process observed under the experimental conditions is

$$Ni^{II}L + X \underset{}{\overset{K}{\rightleftharpoons}} \underset{\text{ion pair}}{\{Ni^{II}L,X\}} \qquad (19)$$

$$\underset{\text{ion pair}}{\{Ni^{II}L,X\}} \xrightarrow[k_2]{HO_2^{\bullet}} LNi^{III}X(HO_2^-) \qquad (20)$$

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followed by

$$\mathrm{LNi^{III}X(HO_2^-) + X + H_3O^+ \xrightarrow{fast} LNi^{III}X_2 + H_2O_2} \quad (21)$$

where reaction 20 is the rate-determining step. The kinetics of formation of the product according to this scheme obey the following rate law:

$$\mathrm{d[LNi^{III}X_2]}/\mathrm{d}t = k_2K[\mathrm{X}][\mathrm{Ni^{II}L}][\mathrm{HO_2^\bullet}]/(1 + K[\mathrm{X}]) \quad (22)$$

i.e.

$$1/k_{\mathrm{obs}} = 1/k_2K[\mathrm{Ni^{II}L}][\mathrm{X^-}] + 1/k_2[\mathrm{Ni(II)L}] \quad (23)$$

The results were analyzed using the technique of repetitive iterations by Marquardt's algorithm[31] to get K and k_2. The results are summed up in Figures 4 and 6 where the points are the experimental results and the lines are the calculated lines using the calculated rate constants. It was found that for the results to coincide with rate law 23 we had to subtract from k_{obs} a constant of 140 ± 50; this contribution to k_{obs} can be attributed to the contribution of the competitive biradical reaction 1 ($k_1 \approx 4 \times 10^6$ $\mathrm{M^{-1}\ s^{-1}}$[8] and $[\mathrm{HO_2^\bullet}] \approx 2 \times 10^{-5}$ M). The results clearly indicate that the experimental findings are in accord with rate law 23. The ionic strength was not kept constant in these experiments due to two reasons: (a) Perchlorate is probably the only common anion which does not act as an axial ligand of $\mathrm{NiL(H_2O)_2^{3+}}$; however, it precipitates the $\mathrm{NiL^{2+}}$ complex at the concentrations required. (b) Clearly any anion will compete with the anions used in the formation of ion pairs. Thus, the calculations use concentrations instead of activities. The results are summed up in Table I.

In the calculation we neglected in the formate-containing system the equilibrium reaction 24, which clearly also depends on the ionic strength; therefore, it is reasonable to expect that the value of K is somewhat higher than calculated in this system.

$$\mathrm{HCO_2^- + H_3O^+ \rightleftharpoons HCO_2H} \quad (24)$$

Sulfate as an Axial Ligand. Air- or oxygen-saturated solutions containing (1–10) × 10^{-4} M $\mathrm{NiL(ClO_4)_2}$, 5 × 10^{-3} M $\mathrm{HCO_2Na}$, and 0.02–1.5 M NaX (where X = $\mathrm{SO_4^{2-}}$) at pH 3.5 were irradiated, and the formation of $\mathrm{Ni^{III}LX_2}$ was observed. The rate of formation of the latter complex was followed at 310 nm where it has a strong absorption band. A process obeying a first-order rate law was observed; this process is pseudo-first-order in $\mathrm{Ni^{II}L}$, Figure 7. The rate also depends on $[\mathrm{SO_4^{2-}}]$, Figure 8, and on the pH but is independent of $[\mathrm{O_2}]$. An experiment to treat the results in parallel with the treatment used in the formate and phosphate systems failed. A different value for the subtraction constants is obtained for each $[\mathrm{Ni^{II}L}]$; the value increases with $[\mathrm{Ni^{II}L}]$. It is therefore suggested that the process observed proceeds via reactions 19 and 20 followed by reaction 21 and in parallel with the following reactions:

$$\mathrm{LNi^{II} + HO_2^\bullet} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \mathrm{L(H_2O)Ni^{III}(HO_2^-)} \quad (25)$$

$$\mathrm{L(H_2O)Ni^{III}(HO_2^-) + X} \xrightarrow[k_4]{\mathrm{fast}} \mathrm{LNi^{III}X(HO_2^-)} \quad (26)$$

$\mathrm{LNi^{III}X(HO_2^\bullet)}$ is the same intermediate as in the mechanism for the formate and phosphate systems, and the final product of this process is $\mathrm{LNi^{III}X_2}$ formed via reaction 21. The rate law derived from this mechanism is

$$\mathrm{d[LNi^{III}X_2]}/\mathrm{d}t = k_2K[\mathrm{X}][\mathrm{Ni^{II}L}][\mathrm{HO_2^\bullet}]/(1 + K[\mathrm{X}]) + k_3[\mathrm{Ni^{II}L}][\mathrm{HO_2^\bullet}] \quad (27)$$

i.e.

$$1/(k_{\mathrm{obs}} - k_3[\mathrm{Ni^{II}L}]) = 1/k_2K[\mathrm{Ni^{II}L}][\mathrm{X}] + \frac{1}{k_2[\mathrm{Ni^{II}L}]} \quad (28)$$

Table I

	K, $\mathrm{M^{-1}}$	k_2, $\mathrm{M^{-1}\ s^{-1}}$	k_3, $\mathrm{M^{-1}\ s^{-1}}$	subtraction constant, $\mathrm{M^{-1}\ s^{-1}}$
phosphate	0.8 ± 0.1	(3.6 ± 0.2) × 10^7		140 ± 50
formate	1.6 ± 0.2	(1.5 ± 0.1) × 10^7		180 ± 40
sulfate	2.5 ± 0.2	(3.6 ± 0.1) × 10^7	(3.4 ± 0.4) × 10^6	

Table II. Observed Volumes of Activation

	$\Delta V^\ddagger$, $\mathrm{cm^3\ mol^{-1}}$			$\Delta V^\ddagger$, $\mathrm{cm^3\ mol^{-1}}$	
[X], M	$\mathrm{SO_4^{2-}}$	$\mathrm{H_2PO_4^-}$	[X], M	$\mathrm{SO_4^{2-}}$	$\mathrm{H_2PO_4^-}$
0.02	−0.3		1.50	−6.2	
0.05	−1.3	−12.4	2.0		−9.6
0.70	−5.9	−10.7			

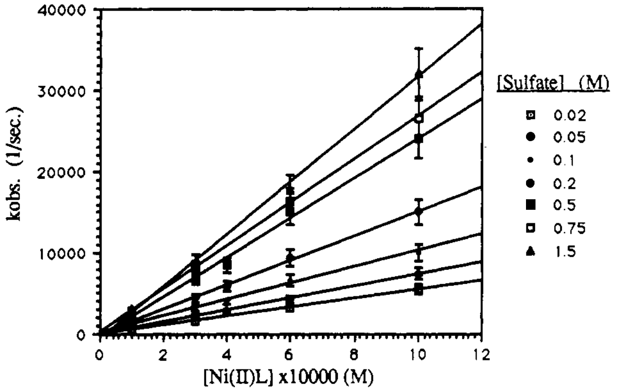

Figure 7. Dependence of the observed rate of formation of $\mathrm{Ni^{III}LX_2}$ on $[\mathrm{Ni^{II}L(ClO_4)_2}]$ in air-saturated solutions at pH 3.5 ● 0.1. Solution composition: $[\mathrm{HCO_2Na}] = 5 \times 10^{-3}$ M, $[\mathrm{Na_2SO_4}]$ = 0.02, 0.05, 0.1, 0.2, 0.5, 0.75, 1.5 M.

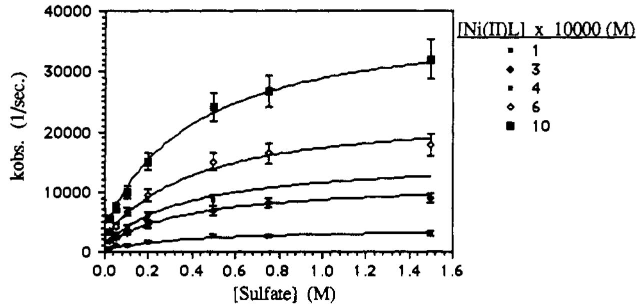

Figure 8. Dependence of the observed rate of formation of $\mathrm{Ni^{III}LX_2}$ on $[\mathrm{Na_2SO_4}]$ in air-saturated solutions at pH 3.5 ± 0.1. Solution composition: $[\mathrm{HCO_2Na}] = 5 \times 10^{-3}$ M, $[\mathrm{Ni^{II}L(ClO_4)_2}] = 1 \times 10^{-4}$, 3×10^{-4}, 4×10^{-4}, 6×10^{-4}, 1×10^{-3} M.

The results were analyzed in the same way that the data were processed in the case of phosphate and formate, Figure 8, but with one exception. Instead of a constant number being subtracted, the subtraction factor depends on the concentration of $\mathrm{Ni^{II}L}$; see Table I.

Measurement of the Volumes of Activation. In order to obtain further insight into the detailed mechanism of these processes, their volumes of activation were determined. For this purpose the overall volumes of activation of the processes observed in the phosphate- and sulfate-containing systems were measured in air-saturated solutions containing 1 × 10^{-3} M $\mathrm{Ni^{II}L(ClO_4)_2}$, 5 × 10^{-3} M $\mathrm{HCO_2Na}$, pH 3.4 ± 0.1, and different concentrations of sulfate and phosphate. Measurements were preformed at four pressures: 0.1, 50, 100, and 150 MPa.

The overall volumes of activation were calculated from a plot of log k_{obs} vs the pressure at different concentrations of sulfate and phosphate, Figure 9. The results are summed up in Table II.

The results at high concentrations of the stabilizing ligand X approach the volumes of activation due to k_2. The measured values of −6.2 ± 1.0 and −9.6 ± 1.0 $\mathrm{cm^3\ mol^{-1}}$ are in accord with expectation for an associative process. Another approach to the

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[31] Marqurdt, D. W. *J. Soc. Ind. Appl. Math.* **1963**, *11* (No. 2).

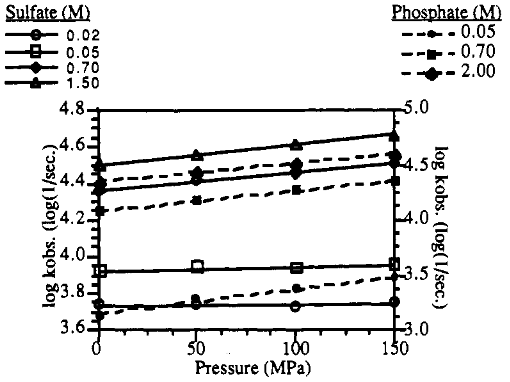


Figure 9. Dependence of the log of the observed first-order rate constant on pressure at different concentrations of sulfate and phosphate. Solution composition: 1×10^{-3} M $Ni^{II}L(ClO_4)_2$, 5×10^{-3} M HCO_2Na, pH 3.4 ± 0.1, air-saturated.

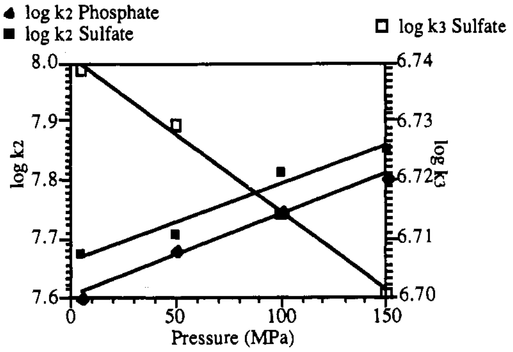


Figure 10. Dependence of log k_2 and log k_3 in the sulfate system and log k_2 in the phosphate system on pressure.

estimation of the volume of activation of k_2 is by using the same analytical technique as before for the calculations of k_2; one calculates k_2 for each pressure. From the slope of the line of log k_2 vs pressure, one calculates the volume of activation for k_2. For sulfate and phosphate, Figure 10, the volumes of activation are −7.2 ± 1.0 and −7.7 ± 1.0 $cm^3\ mol^{-1}$, respectively.

The identical volume of activation for k_2 for the reaction of the ion pair with HO_2 to produce $Ni^{III}LXHO_2$ suggests that the ion pair must be a contact ion pair in which charge neutralization accompanied by desolvation has occurred to a significant extent. If this is not the case, then the binding of HO_2 should be accompanied by such contributions to produce the product which will result in significantly different $\Delta V^{\ddagger}$ values. We therefore concluded that the $\Delta V^{\ddagger}(k_2)$ value of ca. −7 $cm^3\ mol^{-1}$ arises from bond formation of HO_2 with the ion pair, irrespective of the nature of X, i.e., an associatively activated process.

The reaction at low concentrations of the stabilizing ligand X must be a composite of the effect of pressure on K, k_2, and the intercept at low [X]. For $X = H_2PO_4^-$, $\Delta V^{\ddagger}$ becomes significantly more negative at lower [X]. The value of −12.4 $cm^3\ mol^{-1}$ at $[H_2PO_4^-] = 0.05$ M will mainly represent the effect of pressure on Kk_2, i.e., $\Delta\bar{V}(K) + \Delta V^{\ddagger}(k_2)$, since the intercept of 140 ± 50 s^{-1} under these conditions (see Table I and Figure 4) is negligible. It follows that $\Delta\bar{V}(K) \approx -5 \pm 2$ $cm^3\ mol^{-1}$ for $X = H_2PO_4^-$. In the case of $X = SO_4^{2-}$ it was possible to estimate k_3 rather accurately, and from its pressure dependence, Figure 10, $\Delta V^{\ddagger}(k_3) = 1.4 \pm 1.0$ $cm^3\ mol^{-1}$. It follows that the intercept is almost pressure independent, and the measured $\Delta V^{\ddagger}$ data at low $[SO_4^{2-}]$ must again be related to the effect of pressure on Kk_2. In this case $\Delta V^{\ddagger}$ becomes almost zero at low [X], which means that $\Delta\bar{V}(K) \approx 7 \pm 2$ $cm^3\ mol^{-1}$, i.e., ca. 12 $cm^3\ mol^{-1}$ more positive than the corresponding value for $X = H_2PO_4^-$. This once again demonstrates that we are dealing with the formation of a contact ion pair, for which $\Delta\bar{V}(K)$ will consist of an intrinsic volume collapse due to the overlap of the ionic spheres, and an electrostrictive volume increase due to charge neutralization which is accompanied by desolvation.[32] Typical reaction volumes for the interaction of a 2+ charged metal ion with a 1− charged nucleophile are approximately 10–15 $cm^3\ mol^{-1}$ more negative than for the interaction of 2+ and 2− charged species.[32,33] For instance the reaction volume for

$$Ni^{2+}_{aq} + SO_4{}^{2-}{}_{aq} \rightarrow NiSO_{4\,aq} \qquad (29)$$

has a volume between 7 and 10 $cm^3\ mol^{-1}$,[33] which is in excellent agreement with the value of $\Delta\bar{V}(K)$ found in this study.

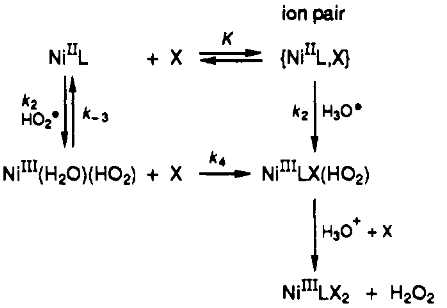
The above quoted value of $\Delta V^{\ddagger}(k_3)$ suggests a dissociative interchange mechanism. This result seems somewhat surprising as $Ni^{II}L_{aq}$ is a planar low-spin complex and reaction 25 as written is an associative process that leads to the formation of a low-spin octahedral complex. This result should be compared to the value published for the volume of activation of reaction 30, which is $\Delta V^{\ddagger}_{30} \cong 4$ $cm^3\ mol^{-1}$.[34]

$$Ni^{II}L + {}^{\bullet}CH_3 \underset{k_{30}}{\rightleftharpoons} L(H_2O)Ni^{III}CH_3 \qquad (30)$$

The volumes of activation of the two equivalent reactions seem to suggest that two water molecules, though not bound to the nickel, occupy the cavities formed by the ligand. These water molecules produce a steric barrier for the radical to approach the metal center; thus, one water molecule has to be partially extricated from the cavity prior to the reaction of the radical with the nickel. Such a mechanism explains the small positive volume of activation for the two reactions.

Thus, the mechanism of oxidation of NiL^{2+} by HO_2 in the sulfate-containing system may be summed up by Scheme I.

Scheme I



As the formation of $Ni^{III}L(H_2O)HO_2$ is not observed in the absence of a stabilizing ligand X, it has to be concluded that $k_3[Ni^{II}L]_{max} \ll k_{-3}$; i.e., $k_{-3} \gg 3.4 \times 10^6 \times 10^{-3} = 3.4 \times 10^3\ s^{-1}$. We therefore estimate that $k_{-3} > 1 \times 10^4\ s^{-1}$. On the other hand, as no effect of $[SO_4^{2-}]$ on the contribution of the k_3-initiated pathway is observed, it has to be concluded that $k_4[SO_4^{2-}]_{min} = k_4 0.02 \gg k_{-3}$. Therefore, $k_4 \gg 1 \times 10^6\ mol^{-1}\ s^{-1}$. Both these estimations are in accord with expectations. As the k_3 pathway is not observed in the formate- and phosphate-containing systems, it has to be concluded that in these systems $k_4[X]_{max} \approx k_4 \ll k_{-3} > 1 \times 10^4$; i.e., k_4 is probably smaller by ca. 2 orders of magnitude in these systems than in the sulfate-containing system.

The volume of activation for the formate system was not measured due to the proximity to the pK_a of formic acid, which could lead to concentration changes caused by the change in pressure.

Concluding Remarks

The results obtained in this study clearly indicate that $HO_2{}^{\bullet}$ free radicals, even those present at pH 7.0 in equilibrium with $O_2{}^{\bullet-}$, can oxidize NiL^{2+} to $Ni^{III}LX_2$ in the presence of a variety of stabilizing ligands. The fact that k_2 is ca. 10 times larger than k_3 indicates that the ion pairs are more susceptible to the $HO_2{}^{\bullet}$ radicals. This difference in reactivity is accompanied by a large difference in $\Delta V^{\ddagger}$, i.e., −7 compared to +1 $cm^3\ mol^{-1}$, which suggests a changeover in mechanism from a dissociative to a more

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(32) Van Eldik, R.; Asano, T.; le Noble, W. J. *Chem. Rev.* **1989**, *89*, 549.
(33) Asano, T.; le Noble, W. J. *Chem. Rev.* **1978**, *78*, 407.
(34) Van Eldik, R.; Cohen, H.; Meshulam, A.; Meyerstein, D. *Inorg. Chem.* **1990**, *29*, 4156.

associative bond formation process on introducing the stabilizing anions. This is most probably related to the totally different solvation shell in the case of NiL^{2+} and $\{NiL^{2+},X\}$ species, which assists the reaction with $HO_2^{\bullet}$ in a more associative way. As the redox potentials of the couples of $Ni^{III}LX_2/NiL^{2+}$ are only somewhat less anodic than that of the $O_2^{\bullet -}/H_2O_2$ couple, most of the oxidizing power of the free radical is maintained in these reactions. If such reactions occur also with transition-metal complexes present in biological systems, the high-valent complexes thus obtained might cause a deleterious process, thus explaining the toxicity of the superoxide.

The detailed mechanism study clearly indicates that the oxidations by $HO_2^{\bullet}$ occur as predicted via the inner-sphere mechanism.

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Supplementary Material Available: Figures 5 and 6, giving rates of formation of $Ni^{III}LX_2$ as a function of the concentrations of $Ni^{II}L(ClO_4)_2$ and HCO_2Na, respectively (2 pages). Ordering information is given on any current masthead page.

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Preparation and ^{31}P NMR Investigations of Monomeric and Dimeric Complexes of Platinum and Palladium with 1,5-Diphosphadithiatetrazocines: X-ray Structure of $Pt(PPh_3)_2(1,5\text{-}Ph_4P_2N_4S_2)\cdot CH_2Cl_2$

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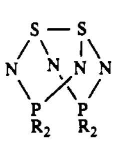
The reaction of $Pt(PPh_3)_2(C_2H_4)$ with $1,5\text{-}R_4P_2N_4S_2$ (R = Ph, Et, Me) in toluene at 23 °C produces the monomeric complexes $Pt(PPh_3)_2(1,5\text{-}R_4P_2N_4S_2)$ (**2a**, R = Ph; **2b**, R = Et; **2c**, R = Me) as air-stable yellow solids, which were characterized by ^{31}P NMR and, in the case of **2a**, ^{195}Pt NMR spectroscopy. The X-ray structure of **2a**$\cdot CH_2Cl_2$ shows that the heterocyclic ligand is bonded to platinum in an η^2-S,S′ fashion with Pt–S distances of 2.408 (4) and 2.341 (4) Å, respectively, and approximately square planar coordination at platinum. The crystals of **2a**$\cdot CH_2Cl_2$ are monoclinic, space group $P2_1/c$, with $a = 22.295$ (2) Å, $b = 10.500$ (1) Å, $c = 24.268$ (2) Å, $\beta = 101.10$ (1)°, $V = 5575$ (1) Å^3, and $Z = 4$. The final R and R_w values were 0.062 and 0.049, respectively. The reaction of $Pd(PPh_3)_4$ with $1,5\text{-}Ph_4P_2N_4S_2$ or $Pd(PPh_2Me)_4$ with $1,5\text{-}R_4P_2N_4S_2$ (R = Ph, Et) in toluene at 23 °C produces $Pd(PPh_3)_2(1,5\text{-}Ph_4P_2N_4S_2)$ or $Pd(PPh_2Me)_2(1,5\text{-}R_4P_2N_4S_2)$, respectively, which were characterized by ^{31}P NMR spectroscopy. Mild heating of the monomeric platinum or palladium complexes, either in solution or in the solid state, results in the dissociation of one of the phosphine ligands to give the dimers $[Pt(PPh_3)(1,5\text{-}R_4P_2N_4S_2)]_2$ (**5a**, R = Ph; **5b**, R = Et) or $[Pd(PPh_2R')(1,5\text{-}R_4P_2N_4S_2)]_2$ (R = R′ = Ph; R′ = Me, R = Ph, Et). The $P_2N_4S_2$ rings in **5a** act as chelating (N,S) ligands toward one platinum and form a bridge to the other platinum via the second sulfur atom to give a centrosymmetric dimeric structure. Variable-temperature ^{31}P NMR spectroscopic investigations of **5a** and **5b** reveal a fluxional process with an interconversion barrier of 10.2 ± 1.2 kcal mol^{-1} for **5a**. A [1,3]-metallotropic rearrangement is proposed to explain this behavior.

Introduction

The combination of hard (N) and soft (S) basic centers bestows upon binary sulfur–nitrogen (S–N) ligands a versatile coordination chemistry, as exemplified by the multifaceted behavior of tetrathiatetrazocine, S_4N_4.[1,2] With zerovalent complexes of the platinum group metals S_4N_4 produces both mono- and dinuclear complexes containing $\overline{\mathrm{MSNSN}}$ rings (M = Pt, Pd, Ni)[3-5] via the unstable adduct $Pt(S_4N_4)(PPh_3)_2$ of unknown structure.[6] The related complexes $Ir(CO)Cl(S_4N_4)(PPh_3)$[7] and $Pt(S_4N_4)Cl_2(PMe_2Ph)_2$[8] incorporate the tridentate (N,S,S) $S_4N_4^{2-}$ ligand formed by insertion of the metal into an S–N bond. By contrast, we have shown that the integrity of 1,5-diphosphadithiatetrazocines (**1**) is retained in the formation of the 1:1 complex $Pt(PPh_3)_2(1,5\text{-}Ph_4P_2N_4S_2)$



1a, R = Ph
1b, R = Et
1c, R = Me

(**2a**),[9] which loses PPh_3 reversibly upon heating in toluene at 105 °C to give the dimer $[Pt(PPh_3)(1,5\text{-}Ph_4P_2N_4S_2)]_2$ (**5a**).[10] The structure of **5a** was shown to involve the ligand **1a** in an (η^2-N,S-μ, η^1-S′) bonding mode,[10] but the structure of **2a** was not established by X-ray crystallography.[9]

In this account we provide the full details of these investigations, which include (a) the preparation and ^{31}P NMR characterization of monomeric platinum complexes $Pt(PPh_3)_2(1,5\text{-}R_4P_2N_4S_2)$ (R = Ph, Et, Me) and palladium complexes $Pd(PPh_2R')_2(1,5\text{-}R_4P_2N_4S_2)$ (R′ = R = Ph; R′ = Me, R = Ph, Et), (b) the preparation and ^{31}P NMR characterization of the corresponding dimers $[Pt(PPh_3)(1,5\text{-}R_4P_2N_4S_2)]_2$ (R = Ph, Et) and $[Pd(PPh_2R')(1,5\text{-}R_4P_2N_4S_2)]_2$, (c) the X-ray crystal structure of the monomer $Pt(PPh_3)_2(1,5\text{-}Ph_4P_2N_4S_2)$ (**2a**), and (d) a discussion

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(1) Chivers, T.; Edelmann, F. *Polyhedron* **1986**, *5*, 1661.
(2) Kelly, P. F.; Woollins, J. D. *Polyhedron* **1986**, *5*, 607.
(3) Ghilardi, C. A.; Midollini, S.; Moneti, S.; Orlandini, A. *J. Organomet. Chem.* **1985**, *286*, 419.
(4) Jones, R.; Kelly, P. F.; Williams, D. J.; Woollins, J. D. *J. Chem. Soc., Chem. Commun.* **1985**, 1325.
(5) Chivers, T.; Edelmann, F.; Behrens, U.; Drews, R. *Inorg. Chim. Acta* **1986**, *116*, 145.
(6) Bhattacharyya, A. A.; McLean, J. A., Jr.; Turner, A. G. *Inorg. Chim. Acta* **1979**, *34*, L199.
(7) Edelmann, F.; Roesky, H. W.; Spang, C.; Noltemeyer, M.; Sheldrick G. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 931.
(8) (a) Hursthouse, M. B.; Motevalli, M.; Kelly, P. F.; Woollins, J. D. *Polyhedron* **1989**, *8*, 997. (b) Kelly, P. F.; Woollins, J. D. *Polyhedron* **1989**, *8*, 2907.
(9) Chivers, T.; Dhathathreyan, K. S.; Ziegler, T. *J. Chem. soc., Chem. Commun.* **1989**, 86.
(10) Chivers, T.; Edwards, M.; Kapoor, P. N.; Meetsma, A.; van de Grampel, J. C.; van de Lee, A. *Inorg. Chem.* **1990**, *29*, 3068.

0020-1669/92/1331-2156$03.00/0