Mechanisms of Reactions of •NO with Complexes with Metal−Carbon σ-Bonds and with Aliphatic Radicals

Sara Goldstein,*,† Dan Meyerstein,‡ and Gidon Czapski†

Department of Physical Chemistry, The Hebrew University of Jerusalem, Jerusalem 91904, Israel, and Chemistry Department, Ben-Gurion University of the Negev, Beer-Sheva, and The College of Judea and Samaria, Kdumim-Ariel, Israel

Received November 27, 1996⊗

The competition kinetics between metal complexes and •NO for aliphatic radicals is a convenient technique for determining the rate constants of the reactions of •NO with aliphatic radicals. Thus, the rate constants of $^\bullet CH_3$ and $^\bullet CH_2OH$ with •NO were determined to be $(3.4 \pm 1.1) \times 10^9$ and $(5.9 \pm 0.5) \times 10^9$ M^{-1} s^{-1}, respectively. The same rate constants can be determined, in several systems, from the decrease in the half-life of transient complexes with metal−carbon σ-bonds which decompose homolytically. In the presence of •NO, the half-life of these transient complexes decreases, and their decomposition turns from second-order to first-order processes. From the dependence of the observed first-order rate constant on •NO and on the metal complex concentrations, it is concluded that the mechanism of the decomposition of these transients in the presence of •NO involves the reaction of •NO with the carbon-centered radicals as well as with the transient with the metal−carbon σ-bonds to form the same products. The rate constants of the reactions of •NO with $(cyclam)(H_2O)Ni^{III}CH_3{}^{2+}$ and $(nta)Co^{III}CH_2OH(H_2O)^-$ were determined to be $(1.5 \pm 0.2) \times 10^5$ and $(3.6 \pm 0.4) \times 10^8$ M^{-1} s^{-1}, respectively. The reactions of •NO with complexes with metal−carbon σ-bonds are analogous to those of aliphatic radicals and dioxygen with the same complexes. This is not surprising as •NO is a radical. The biological implications of these results are discussed.

Introduction

Organometallic complexes are key intermediates in various homogeneous catalytic processes including various biochemical systems.[1−3] Transient complexes with Co−C,[1,2−4] Ni−C,[3,5,6] and Fe−C[3] σ-bonds play an important role in several enzymatic processes. A key step in some of these processes, at least in those catalyzed by Coenzyme B_{12},[2,3] is the homolytic dissociation of the complexes with the metal−carbon σ-bonds.

$$(L{-}M^{(n+1)}{-}R)^{n+} \rightleftharpoons L{-}M^{n+} + R^\bullet \qquad (1)$$

It is therefore of interest to investigate the factors which might affect the mechanism and kinetics of the decomposition of complexes with metal−carbon σ-bonds in biological systems.

•NO has become in the last few years one of the most studied and fascinating molecules in biological chemistry.[7] •NO is generated from L-arginine by the enzyme NO synthase[8] and is involved in a large number of diverse biological processes.[8−11] The most important reactions of •NO in biological systems are those with dioxygen in its various redox forms and with transition metal ions.[12] •NO readily forms complexes with transition metal ions, including those regularly found in metalloproteins. Many of these metal nitrosyls are best regarded as NO^+-adduct complexes.[12]

In this study, the reaction of •NO with complexes with cobalt− and nickel−carbon σ-bonds was investigated. The transition metal complexes which were used do not react with •NO to form NO^+-adduct complexes. The results show that •NO enhances the rate of the decomposition of complexes with metal−carbon σ-bonds either through a direct reaction with the transient complexes or through the reaction with the carbon-centered radical.

Experimental Section

Chemicals. All chemicals were of analytical grade and were used as received. Solutions were prepared with distilled and purified water using a Milli-Q water purification system. $Ni(cyclam)(ClO_4)_2$ was prepared according to literature methods.[13] (Nitrilotriacetato)cobalt(II), $Co^{II}(nta)(H_2O)_2{}^-$, was prepared by mixing $CoSO_4{\cdot}7H_2O$ with a small excess of nitrilotriacetic acid, disodium salt (Sigma). Nitric oxide, CP (Matheson Gas Products), was purified by being passed through a series of scrubbing bottles containing 50% NaOH and purified water in this order. The solutions in the traps were first deaerated by purging with He. Nitric oxide solutions were prepared in gas-tight syringes by purging first water with He to remove O_2, followed by bubbling for 30 min with •NO. •NO-saturated solutions (1.8 mM at 21 °C and 690 mmHg,[14] which is the barometric pressure in Jerusalem) were stored

---

* To whom all correspondence should be delivered. Tel: 972-2-6586478. Fax: 972-2-6586925. E-mail: SARAG@HUJI.VMS.AC.IL.

† The Hebrew University of Jerusalem.

‡ Ben-Gurion University of the Negev, Beer-Sheva, and The College of Judea and Samaria, Kdumim-Ariel.

⊗ Abstract published in *Advance ACS Abstracts*, May 15, 1997.

(1) Espenson, J. H. In *Inorganic and Bioinorganic Mechanisms*; Sykes, A. J., Ed.; Academic Press: London, 1982; Vol. 1, p 1.
(2) Sigel, H.; Sigel, A. *Metals in Biological Systems*; M. Dekker: New York, 1988.
(3) Commack, R. In *Bioinorganic Catalysis*; Reedijk, J., Ed.; M. Dekker: New York, 1993.
(4) Finke, R. G.; Schiraldi, D. A.; Mayer, B. J. *Coord. Chem. Rev.* **1984**, *54*, 1.
(5) Walsh, C. T.; Orme-Johnson, W. H. *Biochemistry* **1987**, *26*, 4901.
(6) Hollinger, C.; Pierick, A. J.; Reijerse, E. J.; Hagen, W. R. *J. Am. Chem. Soc.* **1993**, *115*, 5651.
(7) Koshland, D. E., Jr. *Science* **1992**, *258*, 1861.
(8) Moncada, S.; Palmer, R. M. J.; Higgs, E. A. *Pharmacol. Rev.* **1991**, *43*, 109.
(9) Palmer, R. M. J; Ferrige, A. G.; Moncada, S. *Nature* **1987**, *327*, 524.
(10) Benjamin, N.; Dutton, J. A. E.; Ritter, J. M. *Br. J. Pharmacol.* **1991**, *102*, 847.
(11) Curran, R. D.; Ferrari, F. K.; Kispert, P. H.; Stadler, J.; Stuehr, D. J.; Simmons, R. L.; Billiar, T. R. *FASEB J.* **1991**, *5*, 2085.
(12) Stamler, J. S.; Singel, D. J.; Loscalzo, J. *Science* **1992**, *258*, 1898.
(13) Bosnich, B.; Tobe, M. L.; Webb, G. A. *Inorg. Chem.* **1965**, *4*, 1109.
(14) *Lange's Handbook of Chemistry*, 13th ed.; Dean, J. A., Ed.; McGraw-Hill: New York; p 10−5.

S0020-1669(96)01432-2 CCC: $14.00

in syringes and subsequently diluted with N_2O-saturated solutions to the desired concentrations by the syringe technique.

No spectroscopic changes were observed when neutral deaerated solutions of 2 mM $Ni(cyclam)^{2+}$ and $Co^{II}(nta)(H_2O)_2^-$ were mixed with $^{\bullet}NO$-saturated solutions at a ratio of 1:1 using a stopped flow, indicating that under these conditions $^{\bullet}NO$ does not bind or react with these complexes.

Methods. Pulse radiolysis experiments were carried out with the Varian 7715 linear accelerator with 5-MeV electron pulses of 0.1−1.5 μs and 200-mA current. The dose per pulse was 3−29 Gy, respectively, and was determined with either the thiocyanate dosimeter (10 mM KSCN in N_2O-saturated water) or the hexacyanoferrate(II) dosimeter (5 mM $K_4Fe(CN)_6$ in N_2O-saturated water) using $G\epsilon((SCN)_2^{\bullet-}) = 5.0 \times 10^4\ M^{-1}\ cm^{-1}$ at 475 nm and $G\epsilon(Fe(CN)_6^{3-}) = 6.7 \times 10^3\ M^{-1}\ cm^{-1}$ at 420 nm.[15] A 200-W Xe−Hg or 150-W Xe lamp produced the analyzing light. Appropriate filters were used to minimize photochemical activity. Irradiation was carried out in a 4-cm Spectrosil cell using three light passes.

The transient complexes with the metal−carbon σ-bonds were produced by irradiation of N_2O-saturated aqueous solutions ($[N_2O] \geq 0.02$ M) containing DMSO or CH_3OH, the metal complex, and $^{\bullet}NO$. At pH ≥ 3, the following reactions take place:

$$H_2O \rightarrow e^-_{aq}\ (2.6),\ ^{\bullet}OH\ (2.7),\ H^{\bullet}\ (0.6),\ H_2\ (0.45),\ H_2O_2\ (0.7),\ H_3O^+\ (2.6) \tag{2}$$

(The numbers in parentheses are *G*-values, which represent the number of molecules formed per 100 eV of energy absorbed by pure water.)

The solute concentrations were such that e^-_{aq} reacts with N_2O to produce $^{\bullet}OH$ through reaction 3, and $^{\bullet}OH$ reacts with DMSO or CH_3OH to produce $^{\bullet}CH_3$ and $^{\bullet}CH_2OH$, respectively. The $^{\bullet}H$ radicals are only a small fraction (∼10%) of the total radicals, and they react with the organic compounds and $^{\bullet}NO$.[16] These reactions were complete before the reaction of interest took place.

$$e^-_{aq} + N_2O \rightarrow N_2 + OH^- + OH^{\bullet} \qquad k_3 = 9.1 \times 10^9\ M^{-1}\ s^{-1}\ \text{(ref 16)} \tag{3}$$

$$^{\bullet}OH + (CH_3)_2SO \rightarrow (CH_3)_2\dot{S}OOH \qquad k_4 = 7.0 \times 10^9\ M^{-1}\ s^{-1}\ \text{(ref 16)} \tag{4}$$

$$(CH_3)_2\dot{S}OOH \rightarrow CH_3SOOH + {}^{\bullet}CH_3 \qquad k_5 = 1.5 \times 10^7\ s^{-1}\ \text{(ref 16)} \tag{5}$$

$$CH_3OH + {}^{\bullet}OH \rightarrow {}^{\bullet}CH_2OH + H_2O \qquad k_6 = 9.7 \times 10^8\ M^{-1}\ s^{-1}\ \text{(ref 16)} \tag{6}$$

Results and Discussion

The $Co^{II}(nta)(H_2O)_2^-$/DMSO/$^{\bullet}NO$ System. In previous studies[17,18] it was reported that methyl radicals react with $Co^{II}(nta)(H_2O)_2^-$ to form a long-lived intermediate at pH 4−9 ($\epsilon_{max}{}^{245} = 14\,000\ M^{-1}\ cm^{-1}$, $\epsilon_{max}{}^{390} = 170\ M^{-1}\ cm^{-1}$, $\epsilon_{max}{}^{600} = 90\ M^{-1}\ cm^{-1}$).[17] The mechanism of the formation and decomposition of this intermediate is given by

$$Co^{II}(nta)(H_2O)_2^- + {}^{\bullet}CH_3 \rightleftharpoons (nta)Co^{III}CH_3(H_2O)^- \tag{7}$$

$$k_7 = 1.6 \times 10^8\ M^{-1}\ s^{-1}\ \text{(ref 17)},\ k_{-7} = 57 \pm 6\ s^{-1}\ \text{(ref 18)}$$

$$(nta)Co^{III}CH_3(H_2O)^- + {}^{\bullet}CH_3 \rightarrow C_2H_6 + Co^{II}(nta)(H_2O)_2^- \tag{8}$$

$$k_8 = (3.7 \pm 0.5) \times 10^8\ M^{-1}\ s^{-1}\ \text{(refs 17, 18)}$$

When 14−216 μM $^{\bullet}NO$ was added to N_2O-saturated solutions containing 0.2−5 mM $CoSO_4{\cdot}H_2O$, 6 mM nta, 0.2−0.8 M DMSO, pH 4.5−7.3, and the solutions were irradiated, the formation and decay of $(nta)Co^{III}CH_3(H_2O)^-$ were followed at 270 nm ($\epsilon_{270} \sim 3500\ M^{-1}\ cm^{-1}$)[17]. The yield of the transient decreased with the increase in [$^{\bullet}NO$] and with the decrease in [$Co^{II}(nta)(H_2O)_2^-$] (Figure 1), due to the competition between $Co^{II}(nta)(H_2O)_2^-$ (reaction 7) and $^{\bullet}NO$ (reaction 9) for $^{\bullet}CH_3$. Thus, the yield of the transient is given by eq 10, and plots of 1/OD_{270} vs [$^{\bullet}NO$] and vs 1/[$Co^{II}(nta)(H_2O)_2^-$] yield straight lines with the same intercept (Figure 1). From the slopes and intercepts of the lines in Figure 1, we determined $k_9/k_7 = 25.6 \pm 0.9$, and for $k_7 = 1.6 \times 10^8\ M^{-1}\ s^{-1}$,[17] $k_9 = (4.1 \pm 0.4) \times 10^9\ M^{-1}\ s^{-1}$ was calculated.

$$^{\bullet}NO + {}^{\bullet}CH_3 \rightarrow CH_3NO \tag{9}$$

$$OD_{270} = OD_{270}(max)k_7[Co^{II}(nta)(H_2O)_2^-]/(k_7[Co^{II}(nta)(H_2O)_2^-] + k_9[^{\bullet}NO]) \tag{10}$$

In the presence of $^{\bullet}NO$, the second-order decay of $(nta)Co^{III}CH_3(H_2O)^-$ was replaced by a first-order decay, which was subsequently followed by a slow and relatively small first-order formation of absorption. The observed first-order rate constant of the decay of the absorbance increased with the increase in [$^{\bullet}NO$] and varied inversely with [$Co^{II}(nta)(H_2O)_2^-$] (Figure 2). The rate of the second process was independent of $^{\bullet}NO$ and $Co^{II}(nta)(H_2O)_2^-$ concentrations with $k = 1.7 \pm 0.2\ s^{-1}$.

These results suggest that the decrease in the half-life of $(nta)Co^{III}CH_3(H_2O)^-$ in the presence of $^{\bullet}NO$ is due to reaction 9, and the rate law of the decay is given by eq 11, assuming a steady state for $^{\bullet}CH_3$:

$$\frac{-d[(nta)Co^{III}CH_3(H_2O)^-]}{dt} = \frac{k_9k_{-7}[^{\bullet}NO][(nta)Co^{III}(CH_3)(H_2O)^-]}{k_7[Co^{II}(nta)(H_2O)_2^-] + k_9[^{\bullet}NO]} = k_{obs}[(nta)Co^{III}(CH_3)(H_2O)^-] \tag{11}$$

where

$$\frac{1}{k_{obs}} = \frac{1}{k_{-7}} + \frac{k_7[Co^{II}(nta)(H_2O)_2^-]}{k_{-7}k_9[^{\bullet}NO]} \tag{12}$$

In Figure 2, 1/k_{obs} is plotted vs [$Co^{II}(nta)(H_2O)_2^-$] and vs 1/[$^{\bullet}NO$]. From the intercepts of the lines in the figure, $k_{-7} = 77 \pm 6\ s^{-1}$ was calculated, which is in good agreement with the earlier reported value of $56 \pm 6\ s^{-1}$.[18] From the slopes and intercepts of these lines, $k_9 = (3.7 \pm 0.4) \times 10^9\ M^{-1}\ s^{-1}$, which is in excellent agreement with the value determined from the dependence of the initial yields of the transient on $^{\bullet}NO$ and $Co^{II}(nta)(H_2O)_2^-$ concentrations (Figure 1).

The second process is attributed to the isomerization of CH_3NO to $CH_2{=}NOH$ as it is known that nitroso compounds are

---

[15] Buxton, G. V.; Stuart, C. R. *J. Chem. Soc., Faraday Trans.* **1995**, *91*, 279.

[16] Ross, A. B.; Mallard, W. G.; Helman, W. P.; Buxton, J. V.; Huie, R. E.; Neta, P. *NIST Standard References Database 40, Version 2.0*; 1994.

[17] Meyerstein, D.; Schwarz, H. A. *J. Chem. Soc. Faraday Trans. 1* **1988**, *84*, 2933.

[18] Sauer, A.; Cohen, H.; Meyerstein, D. *Inorg. Chem.* **1989**, *28*, 2511.

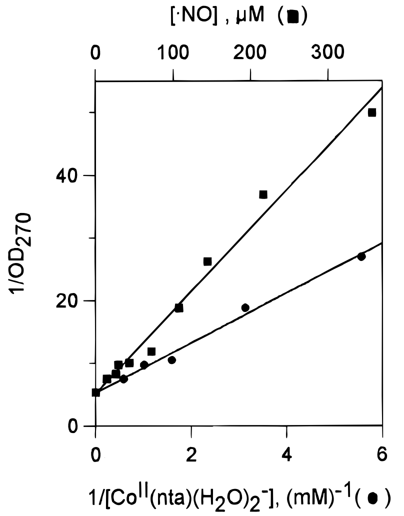


Figure 1. Reciprocal yields of $(nta)Co^{III}CH_3(H_2O)^-$ measured 100 μs after the end of the pulse as a function of $[^{\bullet}NO]$ in the presence of 1 mM $Co^{II}(nta)(H_2O)_2^-$ and as a function of $1/[Co^{II}(nta)(H_2O)_2^-]$ in the presence of 28 μM $^{\bullet}NO$. All solutions contained 0.2 M DMSO at pH 7.2 ± 0.1.

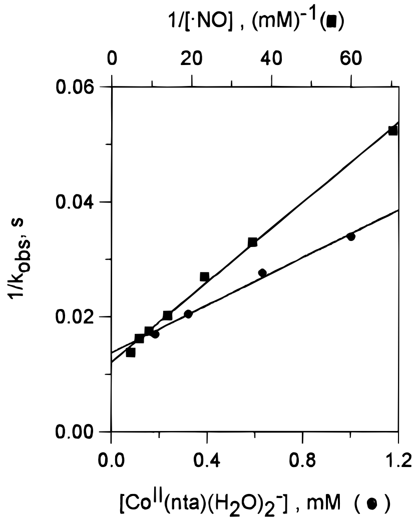


Figure 2. Reciprocal of the observed first-order rate constants of the decay of $(nta)Co^{III}CH_3(H_2O)^-$ as a function of $1/[^{\bullet}NO]$ in the presence of 1 mM $Co^{II}(nta)(H_2O)_2^-$ and as a function of $[Co^{II}(nta)(H_2O)_2^-]$ in the presence of 28 μM $^{\bullet}NO$. All solutions contained 0.2 M DMSO at pH 7.2 ± 0.1.

unstable and undergo dimerization or isomerization to oximes.[19] As the observed process is first order, it is assumed that CH_3NO mainly isomerizes to $CH_2{=}NOH$. This assumption was verified by irradiation of the same solutions without the metal complex. Under these conditions reactions 2−5 and 9 take place and are complete within a few microseconds. Yet, a first-order formation at 270 nm was observed with $k = 0.9 \pm 0.1\ s^{-1}$, which is somewhat slower than the observed one in the presence of the metal complex.

The $Co^{II}(nta)(H_2O)_2^-/CH_3OH/^{\bullet}NO$ System. It has been reported that $^{\bullet}CH_2OH$ reacts with $Co^{II}(nta)(H_2O)_2^-$ at pH 4 to form $(nta)Co^{III}CH_2OH(H_2O)^-$ ($\epsilon_{max}^{256} = 9300\ M^{-1}\ cm^{-1}$, $\epsilon_{max}^{396} = 310\ M^{-1}\ cm^{-1}$, $\epsilon_{max}^{600} = 30\ M^{-1}\ cm^{-1}$), which decays according to the same mechanism given for $(nta)Co^{III}CH_3(H_2O)^-$.[17]

$$Co^{II}(nta)(H_2O)_2^- + {}^{\bullet}CH_2OH \rightleftharpoons (nta)Co^{III}CH_2OH(H_2O)^- \quad (13)$$

$$(nta)Co^{III}CH_2OH(H_2O)^- + {}^{\bullet}CH_2OH \rightarrow (CH_2OH)_2 + Co^{II}(nta)(H_2O)_2^- \quad (14)$$

When N_2O-saturated solutions containing 0.5−5 mM $CoSO_4{\cdot}7H_2O$, 6 mM nta, 0.2−0.5 M CH_3OH, 8.5−72 μM $^{\bullet}NO$, pH 4, were irradiated, the formation and decay of $(nta)Co^{III}CH_2OH(H_2O)^-$ were followed at 270 nm ($\epsilon \sim 5000\ M^{-1}\ cm^{-1}$).[17] The yield of the transient decreased with the increase in $[^{\bullet}NO]$ and with the decrease in $[Co^{II}(nta)(H_2O)_2^-]$ (Figure 3), demonstrating a competition between $Co^{II}(nta)(H_2O)_2^-$ (reaction 13) and $^{\bullet}NO$ (reaction 15) for $^{\bullet}CH_2OH$. From the intercepts and slopes of the lines in Figure 3 (see above as in the case of DMSO), $k_{15} = (5.9 \pm 0.5) \times 10^9\ M^{-1}\ s^{-1}$ was determined.

$$^{\bullet}NO + {}^{\bullet}CH_2OH \rightarrow HOCH_2NO \quad (15)$$

In the presence of $^{\bullet}NO$, the absorbance decayed via three subsequent first-order reactions (Figure 4). The observed first-order rate constant of the first decay of $(nta)Co^{III}CH_2OH(H_2O)^-$ at relatively high $[Co^{II}(nta)(H_2O)_2^-]$ (5 mM) was linearly dependent on $[^{\bullet}NO]$, (Figure 5a) and, at lower concentrations, slightly depended inversely on $[Co^{II}(nta)(H_2O)_2^-]$, e.g., when the concentration of $Co^{II}(nta)(H_2O)_2^-$ decreased from 5 mM to 0.5 mM in the presence of 43 μM $^{\bullet}NO$, k_{obs} increased from 1.6×10^4 to $2.3 \times 10^4\ s^{-1}$. The two other subsequent first-order decays were independent of $[^{\bullet}NO]$ and of $[Co^{II}(nta)(H_2O)_2^-]$, with $k = 310 \pm 50$ and $0.09 \pm 0.02\ s^{-1}$.

These results demonstrate that the decrease in the half-life of $(nta)Co^{III}CH_2OH(H_2O)^-$ in the presence of $^{\bullet}NO$ is due to reactions 15 and 16, where $k_{16} = (4.0 \pm 0.3) \times 10^8\ M^{-1}\ s^{-1}$ was determined from the slope of the line in Figure 5.

$$(nta)Co^{III}CH_2OH(H_2O)^- + {}^{\bullet}NO \rightarrow Co^{II}(nta)(H_2O)_2^- + HOCH_2NO \quad (16)$$

According to reactions 13−16, k_{obs} of the decay of $(nta)Co^{III}CH_2OH(H_2O)^-$ is given by eq 17, assuming a steady state for $^{\bullet}CH_2OH$. Thus, a plot of $k_{obs}/[^{\bullet}NO]$ vs $k_{15}/(k_{15}[^{\bullet}NO]$

$$k_{obs} = k_{16}[^{\bullet}NO] + \frac{k_{15}k_{-13}[^{\bullet}NO]}{k_{15}[^{\bullet}NO] + k_{13}[Co^{II}(nta)(H_2O)_2^-]} \quad (17)$$

$+\ k_{13}[Co^{II}(nta)(H_2O)_2^-])$ should yield a straight line with intercept $= k_{16}$ and slope $= k_{-13}$. The results are in good agreement with this suggested mechanism (Figure 6). From the intercept and slope of the line in Figure 6, $k_{16} = (3.2 \pm 0.2) \times 10^8\ M^{-1}\ s^{-1}$ and $k_{-13} = (1.4 \pm 0.1) \times 10^4\ s^{-1}$ were determined. The value of k_{16} is in good agreement with that determined directly (Figure 5a). The determined value of k_{-13} is lower than the earlier reported one, $3.9 \times 10^4\ s^{-1}$.[17] We believe that our value is better as the earlier one was calculated by assuming that $2k_{14} = 1 \times 10^9\ M^{-1}\ s^{-1}$.[17]

The other two first-order processes are attributed to the instability of $HOCH_2NO$, which isomerizes to $HOCH{=}NOH$ and subsequently hydrolyzes to HCONHOH. This assumption was verified by observing these two processes at 270 nm when the same solutions without the metal complex were irradiated. Under these conditions reactions 2, 3, 6, and 15 take place and are complete within a few microseconds. Two first-order decays were observed with $k = 260 \pm 60$ and $0.05 \pm 0.01\ s^{-1}$, which

---

(19) William, D. H. L. In *Nitrosation*; Cambridge University Press: Cambridge, 1988.

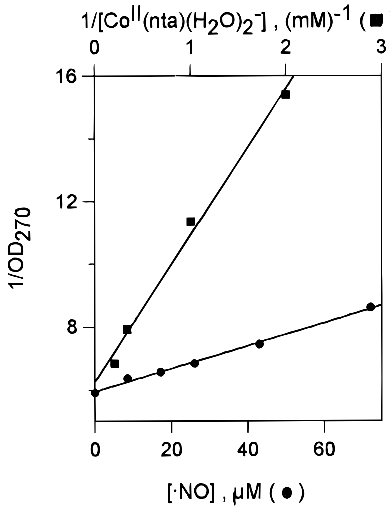


Figure 3. Reciprocal yields of $(nta)Co^{III}CH_2OH(H_2O)^-$ measured at the end of the formation process (2−15 μs after the end of the pulse) as a function of $[{}^{\bullet}NO]$ in the presence of 5 mM $Co^{II}(nta)(H_2O)_2^-$ and as a function of $1/[Co^{II}(nta)(H_2O)_2^-]$ in the presence of 26 μM ${}^{\bullet}NO$. All solutions contained 0.5 M CH_3OH at pH 4.

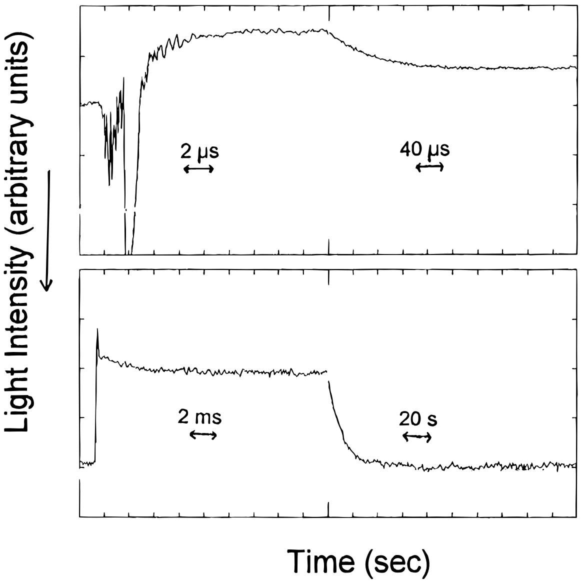


Figure 4. Kinetic traces obtained when N_2O-saturated solutions containing 1 mM $Co^{II}(nta)(H_2O)_2^-$, 28 μM ${}^{\bullet}NO$, and 0.2 M CH_3OH at pH 4 were irradiated. ($I_0 = -662$ mV, ΔV_1 (formation) = 101 mM, ΔV_2 (first decay) = 50 mV, ΔV_3 (second decay) = 61 mV, ΔV_4 (third decay) = 41 mV, $\lambda = 270$ nm, $l = 12.1$ cm).

are in fair agreement with the values determined in the presence of the metal complex.

The $Ni^{II}(cyclam)^{2+}/DMSO/{}^{\bullet}NO$ System. The mechanism of the formation of $(cyclam)(H_2O)Ni^{III}CH_3^{2+}$ at pH 3 was reported to be identical to that of $(nta)Co^{III}CH_3(H_2O)^-$ at pH 4−9, but $k_{18} = (6.5 \pm 0.7) \times 10^8$ M^{-1} s^{-1}, $k_{-18} = 57 \pm 6$ s^{-1}, and $k_{19} = 4 \times 10^7$ M^{-1} s^{-1}.[20]

$$Ni^{II}(cyclam)^{2+} + {}^{\bullet}CH_3 \rightleftharpoons (cyclam)(H_2O)Ni^{III}CH_3^{2+} \quad (18)$$

$$(cyclam)(H_2O)Ni^{III}CH_3^{2+} + {}^{\bullet}CH_3 \rightarrow C_2H_6 + Ni^{II}(cyclam)^{2+} \quad (19)$$

When 28−288 μM ${}^{\bullet}NO$ was added to N_2O-saturated solutions containing 0.08−1 mM $Ni^{II}(cyclam)^{2+}$, 0.1−0.8 M DMSO, pH 3, and the solutions were irradiated, the formation and decomposition of $(cyclam)(H_2O)Ni^{III}CH_3^{2+}$ were followed at 300 nm ($\epsilon_{max}^{300} = 1900$ M^{-1} cm^{-1})[20]. The yield of the intermediate decreased with the increase in $[{}^{\bullet}NO]$ and the decrease in $[Ni^{II}(cyclam)^{2+}]$, and plots of $1/OD_{300}$ vs $[{}^{\bullet}NO]$ and vs $1/[Ni^{II}(cyclam)^{2+}]$ yielded straight lines with the same intercept (data not shown). From the slopes and intercepts of these lines, we determined $k_9/k_{18} = 4.0 \pm 0.4$, and as $k_{18} = (6.5 \pm 0.7) \times 10^8$ M^{-1} s^{-1}, $k_9 = (2.6 \pm 0.6) \times 10^9$ M^{-1} s^{-1} was calculated.

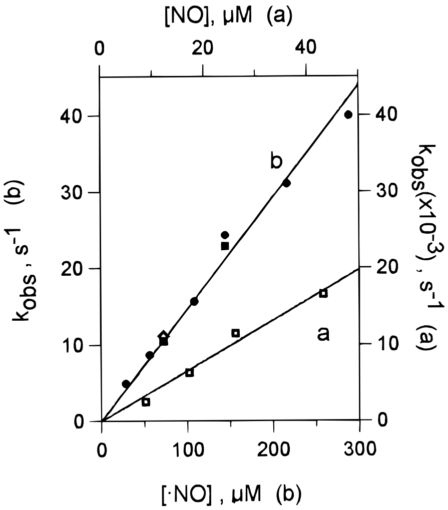


Figure 5. k_{obs} of the decay of $(L-M^{(n+1)}-R)^{n+}$ as a function of $[{}^{\bullet}NO]$ in the presence of (a) 5 mM $Co^{II}(nta)(H_2O)_2^-$ and 0.5 M CH_3OH at pH 4 and (b) 0.1 M DMSO at pH 3 and (●) 1 mM, (■) 0.2 mM, and (△) 0.08 mM $Ni(cyclam)^{2+}$.

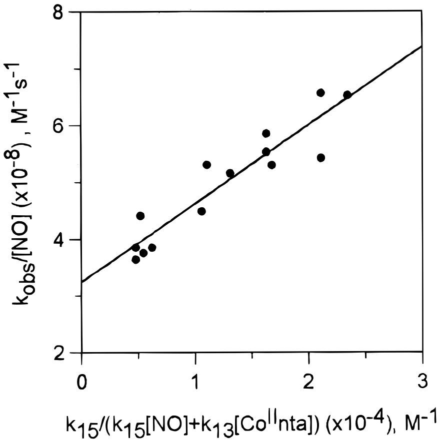


Figure 6. $k_{obs}/[{}^{\bullet}NO]$ as a function of $k_{15}/(k_{15}[{}^{\bullet}NO] + k_{13}[Co^{II}(nta)(H_2O)_2^-])$ for $k_{15} = 5.9 \times 10^9$ M^{-1} s^{-1} and $k_{13} = 2.0 \times 10^8$ M^{-1} s^{-1}. All solutions contained 0.5 M methanol at pH 4.

In contrast to $(nta)Co^{III}CH_3(H_2O)^-$, the observed first-order decay of $(cyclam)(H_2O)Ni^{III}CH_3^{2+}$ was linearly dependent on $[{}^{\bullet}NO]$ and was independent of $[Ni^{II}(cyclam)^{2+}]$ (Figure 5b). We, therefore, assume that in this system the decrease in the half-life of $(cyclam)(H_2O)Ni^{III}CH_3^{2+}$ in the presence of ${}^{\bullet}NO$ is mainly due to reaction 20, and k_{20} was determined from the slope of the line in Figure 5b to be $(1.5 \pm 0.2) \times 10^5$ M^{-1} s^{-1}.

$$(cyclam)(H_2O)Ni^{III}CH_3^{2+} + {}^{\bullet}NO \rightarrow Ni^{II}(cyclam)^{2+} + CH_3NO \quad (20)$$

A similar behavior was found when $Cr(H_2O)_6^{2+}$ replaced ${}^{\bullet}NO$.[20] Under these conditions k_{obs} of the decomposition of $(cyclam)(H_2O)Ni^{III}CH_3^{2+}$ was linearly dependent on $[Cr(H_2O)_6^{2+}]$ and independent of $[Ni^{II}(cyclam)^{2+}]$, resulting in $k(LNi^{III}CH_3^{2+}+Cr^{2+}) = 1.1 \times 10^5$ M^{-1} s^{-1}.[20]

---

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

We have shown that $^{\bullet}$NO reacts rapidly with both (cyclam)(H_2O)$Ni^{III}CH_3{}^{2+}$ and $^{\bullet}CH_3$. Therefore, k_{obs} of the the decomposition of (cyclam)(H_2O)$Ni^{III}CH_3{}^{2+}$ is given by eq 21, assuming a steady state for $^{\bullet}CH_3$. We found that k_{obs} was independent

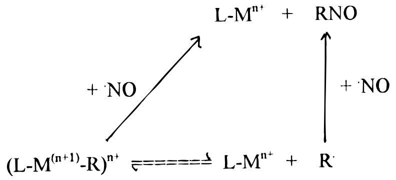
$$k_{obs} = k_{18}[^{\bullet}NO] + \frac{k_9 k_{-18}[^{\bullet}NO]}{k_9[^{\bullet}NO] + k_{18}[Ni^{II}(cyclam)^{2+}]} \qquad (21)$$

of [Ni^{II}(cyclam)$^{2+}$] = 0.08−1 mM (Figure 5b). Therefore, the second term in eq 21 can be neglected provided that $k_{-18} < 2$ s^{-1}. This value is lower than the earlier reported value, 57 ± 6 s^{-1}, which has been determined in the presence of O_2, where it was assumed that O_2 reacts only with the methyl radical.[20] The source of this discrepancy is not clear, and it might be proposed that a side reaction in the presence of O_2 contributes to the kinetic rate law. When the previously reported results for the effect of $Cr(H_2O)_6{}^{2+}$ [20] are fitted to eq 21 for $k_{18} = (6.5 \pm 0.7) \times 10^8$ M^{-1} s^{-1} and $k(^{\bullet}CH_3 + Cr(H_2O)_6{}^{2+}) = 2.4 \times 10^8$ M^{-1} s^{-1},[20] a good fit is obtained only for $k_{-18} < 10$ s^{-1}, which is in good agreement with our results.

Conclusions

This study demonstrates that the competition kinetics between metal complexes and $^{\bullet}$NO for aliphatic radicals is a convenient technique for determining the rate constants of the reactions of $^{\bullet}$NO with aliphatic radicals. The rate constants of $^{\bullet}CH_3$ and $^{\bullet}CH_2OH$ with $^{\bullet}$NO were determined to be $(3.4 \pm 1.1) \times 10^9$ and $(5.9 \pm 0.5) \times 10^9$ M^{-1} s^{-1}, respectively, very similar to that of $^{\bullet}$NO with ethyl alcohol radicals, which has been determined directly.[21]

The same rate constants can be determined, in several systems, from the decrease in the half-life of transients with metal−carbon σ-bonds, which decompose homolytically. $^{\bullet}$NO decreases the half-life of complexes with metal−carbon σ-bonds, which decompose homolytically. This effect is due to two alternative competing mechanisms, where $^{\bullet}$NO reacts with the carbon-centered radical and directly with the transient complex to form the same products:



The reactions of $^{\bullet}$NO with transient complexes with metal−carbon σ-bonds are analogous to those of aliphatic radicals and dioxygen with the same complexes. This is not surprising as $^{\bullet}$NO is a radical.

Biologically, the important reactions of $^{\bullet}$NO are those with oxygen in its various redox forms and with transition metal ions to form metal nitrosyls, which are best regarded as NO^+-adduct complexes. In the present study it is shown that $^{\bullet}$NO decreases the half-life of transient complexes with metal−carbon σ-bonds by reacting directly with these transients or with the carbon-centered radicals. Such reactions may play a role in biological systems, e.g., inactivation of coenzyme B_{12}. Such reactions may play an important role even if only a small fraction of $^{\bullet}$NO will react with the coenzyme, as the amount of $^{\bullet}$NO produced in the biological systems exceeds by orders of magnitude the concentrations of the coenzymes.

Acknowledgment. This research was supported by Grant 4129 from The Council For Tobacco Research and by The Israel Science Foundation.

IC9614327

---

(21) Czapski, G.; Holcman, J.; Bielski, B. H. J. *J. Am. Chem. Soc.* **1994**, *116*, 11465.