6632 *Inorg. Chem.* **1996,** *35,* 6632−6633

Nickel Complexes as Antioxidants. Inhibition of Aldehyde Autoxidation by Nickel(II) Tetraazamacrocycles

Wonwoo Nam,*,[†] Seung Joong Baek,[†] Kyoung Ah Lee,[†] Byung Tae Ahn,[†] James G. Muller,[‡] Cynthia J. Burrows,[‡] and Joan Selverstone Valentine*,[§]

Department of Chemistry, Ewha Womans University, Seoul 120-750, Korea, Department of Chemistry, University of Utah,
Salt Lake City, Utah 84112, and Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90095

Received October 24, 1995

In the course of our recent studies of metal complex-mediated epoxidation of olefins by O_2 plus aldehyde with co-oxidation of aldehydes,[1a] we discovered a surprising property of Ni(cyclam)$^{2+}$ and several related tetraazamacrocylic complexes of Ni(II), i.e., the ability to act as a powerful inhibitor of the free-radical autoxidation of aldehydes.[2] We report herein these observations, our studies of this phenomenon, and a proposed mechanism for the observed inhibition.

The epoxidation of cyclohexene by dioxygen with co-oxidation of aldehyde in the presence of most metal cyclam complexes gave high yields of cyclohexene oxide. Earlier work led to the conclusion that acylperoxy radicals, RC(O)OO$^\bullet$, generated in the aldehyde autoxidation reaction, are frequently the species that react with olefins to give epoxides.[1] However, no formation of cyclohexene oxide was observed in the case of the Ni(II) cyclam complex (see Table 1). Moreover, when the Ni(II) cyclam complex was added to the other metal(II) cyclam complex-mediated cyclohexene epoxidations, the oxidations of cyclohexene and the aldehyde no longer began promptly but instead required an initiation period of at least 8 h (see Table 1), clearly indicating that the nickel cyclam complex was inhibiting the oxidation reaction. By contrast, neither the cyclam ligand alone nor nickel nitrate added to the reaction mixture inhibited the iron cyclam-mediated epoxidation reaction. We therefore tested a variety of nickel complexes of tetraazamacrocyclic ligands in the iron cyclam complex-mediated cyclohexene epoxidations and found that the ability of these nickel complexes to inhibit the co-oxidation reaction was related to the reduction potentials of the nickel complexes as shown in Figure 1.[3] The effective inhibitors were those nickel complexes with relatively low Ni^{III}/Ni^{II} reduction potentials (≤0.86 V), whereas nickel complexes with relatively high reduction potentials did not inhibit the oxidation reactions. In other words, the complexes of ligands that tend to stabilize the Ni^{III} oxidation state relative to Ni^{II} were the effective inhibitors.

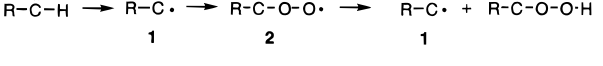
Table 1. Epoxidation of Cyclohexene by O_2 plus Aldehyde in the Absence and Presence of Ni(cyclam)$(NO_3)_2$[a]

metal cyclam complex	yield of cyclohexene oxide (mmol)	metal cyclam complex	yield of cyclohexene oxide (mmol)
Mn(cyclam)$^{2+}$	1.0	Ni(cyclam)$^{2+}$	0.0
Mn(cyclam)$^{2+\,b}$	0.0	Cu(cyclam)$^{2+}$	0.9
Fe(cyclam)$^{2+}$	1.4	Cu(cyclam)$^{2+\,b}$	0.0
Fe(cyclam)$^{2+\,b}$	0.0	Zn(cyclam)$^{2+}$	0.4
Co(cyclam)$^{2+}$	1.6	Zn(cyclam)$^{2+\,b}$	0.0
Co(cyclam)$^{2+\,b}$	0.0	no metal complex	0.4

[a] Reaction conditions: M(cyclam)$^{2+}$ (0.02 mmol), cyclohexene (3 mmol), and cyclohexanecarboxaldehyde (1 mL) in CH_3CN (5 mL). O_2 was bubbled through the reaction solution for 4 h. [b] Same as in footnote *a* except that Ni(cyclam)$^{2+}$ (0.02 mmol) was added to the reaction mixture and that O_2 was bubbled through the reaction solution for 8 h.

An EPR study of the reaction with nickel(II) cyclam and O_2/aldehyde in CH_3CN revealed the presence of an intermediate with an EPR spectrum characteristic of a Ni^{III} species ($g_\perp = 2.190$, $g_\parallel = 2.025$) (see Figure 2).[3a,4] This result indicated that the nickel(II) cyclam complex that was present at the beginning of the reaction was oxidized to give a Ni^{III}-containing species during the oxidation reaction, suggesting that this Ni^{III} species might be the inhibitor. We therefore compared the effect of adding either nickel(II) or nickel(III) cyclam in order to determine which oxidation state of the nickel complex actually has the ability to inhibit the radical chain reaction. The reaction system used was identical to those described in Table 1, except that cobalt(III) acetylacetonate (0.02 mmol) was used in place of the metal cyclam complex and either nickel(II) or nickel(III) cyclam (0.02 mmol) was also added. The reaction carried out in the presence of nickel(II) cyclam did not give any oxidation products for 8 h, whereas the reaction with nickel(III) cyclam yielded the oxidation products as soon as the reaction started. The amount of cyclohexene oxide formed in the latter reaction was similar to that obtained in the reaction with cobalt(III) acetylacetonate alone.[5] The UV−vis spectrum of the reaction mixture demonstrated that the reaction was inhibited during the period when nickel(II) cyclam was being oxidized to nickel(III) cyclam and that the epoxidation reaction began after the oxidation to nickel(III) cyclam was complete. We conclude, therefore, that nickel(II) cyclam rather than nickel(III) cyclam is the true inhibitor of the reaction.

Autoxidation of aldehydes has been studied extensively, and the mechanism is well understood.[2a] The reaction proceeds by a free-radical chain mechanism: First, an initiation step occurs in which a hydrogen atom is removed from the aldehyde, producing an acyl radical, **1**. Then **1** reacts with O_2 to give an acylperoxy radical, **2**. The acylperoxy radical, **2**, acts as a chain carrier by reacting with another aldehyde to produce **1** and a peroxy acid (eq 1).



$$\underset{}{R\text{-}\overset{O}{\overset{\|}{C}}\text{-}H} \xrightarrow{M^{n+}} \underset{\mathbf{1}}{R\text{-}\overset{O}{\overset{\|}{C}}\bullet} \xrightarrow{O_2} \underset{\mathbf{2}}{R\text{-}\overset{O}{\overset{\|}{C}}\text{-}O\text{-}O\bullet} \xrightarrow{RCHO} \underset{\mathbf{1}}{R\text{-}\overset{O}{\overset{\|}{C}}\bullet} + R\text{-}\overset{O}{\overset{\|}{C}}\text{-}O\text{-}O\text{-}H \qquad (1)$$

Inhibition of this chain reaction is most likely to be due to reaction of the inhibitor with one of the chain carriers, i.e., **1** or **2**. Two lines of reasoning lead us to conclude that **2** is the radical intermediate trapped by the nickel complexes: (1) The

---

[†] Ewha Womans University.

[‡] University of Utah.

[§] University of California, Los Angeles.

(1) (a) Nam, W.; Kim, H. J.; Kim, S. H.; Ho, R. Y. N.; Valentine, J. S. *Inorg. Chem.* **1996**, *35*, 1045−1049. (b) An analysis of much of the recent literature on this subject can be found in: Finke, R. G. *J. Mol. Catal.*, in press.

(2) (a) Simandi, L. I., Ed. *Catalytic Activation of Dioxygen by Metal Complexes*; Kluwer Academic Publishers: Dordrecht, 1992; pp 318−331. (b) Sheldon, R. A., Kochi, J. K., Eds. *Metal-Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, 1981; pp 359−363. (c) Nagata, T.; Imagawa, K.; Yamada, T.; Mukaiyama, T. *Chem. Lett.* **1994**, 1259−1262 and references therein.

(3) The Ni^{III}/Ni^{II} reduction potentials for the nickel complexes were obtained from the following papers: (a) Lovecchio, F. V.; Gore, E. S.; Busch, D. H. *J. Am. Chem. Soc.* **1974**, *96*, 3109−3118. (b) Muller, J. G.; Chen, X.; Dadiz, A. C.; Rokita, S. E.; Burrows, C. J. *J. Am. Chem. Soc.* **1992**, *114*, 6407−6411. (c) Fabbrizzi, L.; Poggi, A. *Inorg. Chim. Acta* **1980**, *39*, 207−210.

S0020-1669(95)01365-6 CCC: $12.00

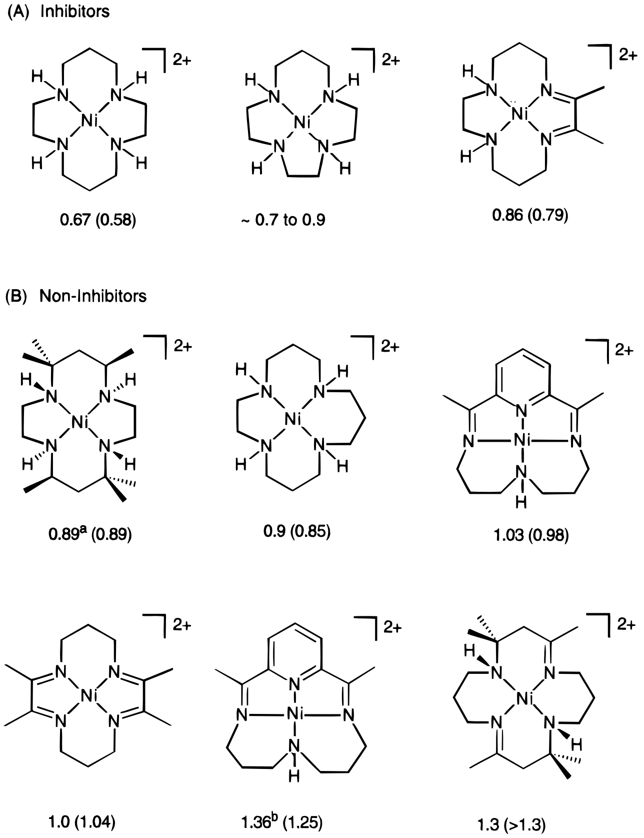


Figure 1. Nickel(II) complexes tested as inhibitors in the iron cyclam-mediated epoxidation of cyclohexene by O_2 plus aldehyde. Reactions in the presence of those complexes identified as inhibitors gave no detectable epoxide in 4 h. Reactions in the presence of those complexes identified as non-inhibitors gave yields of epoxide identical to those observed in their absence. Reaction conditions: nickel complex (0.02 mmol), iron(II) cyclam (0.02 mmol), cyclohexene (3 mmol), and cyclohexanecarboxaldehyde (1 mL) in CH_3CN (5 mL). Reduction potentials in volts versus the Ag−AgCl electrode are given below each compound for acetonitrile[3a] (and in water,[3b] in parentheses, when available). Key: (a) determined in this study; (b) ref 3c.

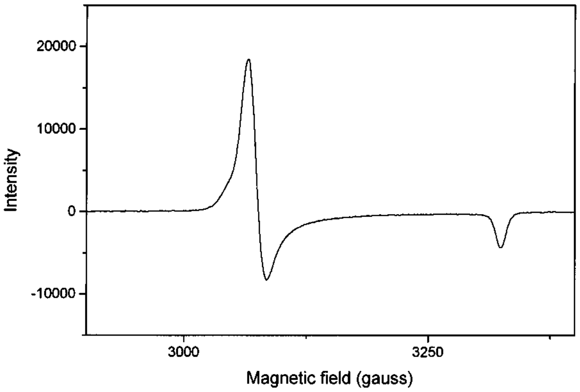
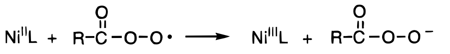


Figure 2. X-band EPR spectrum of the Ni(III) complex formed in the reaction of Ni(cyclam)$^{2+}$ (0.02 mmol) and cyclohexanecarboxaldehyde (1 mL) in CH_3CN (5 mL). The reaction solution was stirred for 5 h under an O_2 atmosphere at room temperature and then frozen for the EPR experiment. Double integration of the signal against a Cu standard (1.0 mM $CuSO_4{\cdot}5H_2O$) indicates the presence of 0.6 spin/Ni. Instrumental parameters: temperature, 77 K; microwave frequency, 9.43 GHz at 5 mW power; modulation amplitude, 9 G; receiver gain, 1000.

reaction of **1** with O_2 to give **2** is known to be extremely fast, and it is unlikely that its rate of reaction with the Ni^{II} complex would be fast enough to compete.[6] (2) The addition of cyclohexene to the reaction mixture of Ni^{II} complex, O_2, and aldehyde was found to delay the initiation of the reaction substantially, suggesting that the olefin and the Ni^{II} complex were scavenging the same intermediate.[1,7] We therefore conclude that nickel complexes with relatively low Ni^{III}/Ni^{II} reduction potentials terminate the radical process by rapidly reducing the acylperoxy radical to a peroxy anion (eq 2), thus



$$\mathrm{Ni^{II}L} + \mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}O{-}O\cdot} \longrightarrow \mathrm{Ni^{III}L} + \mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}O{-}O^-} \qquad (2)$$

2

preventing the accumulation of sufficient concentrations of **2** to propagate the free-radical chain mechanism (eq 1). Why are the Ni^{II} complexes unique as inhibitors of this chain reaction? We believe the reason is that these Ni^{II} complexes are sufficiently good reducing agents to react rapidly with acylperoxy radicals and inhibit the chain reaction but they are not oxidized by dioxygen. Other reducing metal complexes should also be able to inhibit this autoxidation reaction as well, but only if they are likewise inert to oxidation by dioxygen.

Acknowledgment. Financial support for this research from Ewha Womans University (W.N. and B.T.A.), the Ministry of Education of Korea (Grant BSRI-94-3412) (W.N.), and the National Science Foundation (J.S.V. and C.J.B.) is gratefully acknowledged.

IC9513651

---

(4) Zeigerson, E.; Ginzburg, G.; Schwartz, N.; Luz, Z.; Meyerstein, D. *J. Chem. Soc., Chem. Commun.* **1979**, 241−243.

(5) The yield of cyclohexene oxide after 8 h of reaction was 1.6 mmol with cobalt(III) acetylacetonate alone and 1.5 mmol with cobalt(III) acetylacetonate plus nickel(III) cyclam.

(6) (a) Boga, E.; Peintler, G.; Nagypal, I. *J. Am. Chem. Soc.* **1990**, *112*, 151−153. (b) Roelofs, M. G.; Wasserman, E.; Jensen, J. H. *J. Am. Chem. Soc.* **1987**, *109*, 4207−4217.

(7) O_2 was bubbled through the reaction solution containing Ni(cyclam)$^{2+}$ (0.02 mmol) and cyclohexanecarboxaldehyde (1 mL) in CH_3CN (5 mL). The oxidation of aldehyde was initiated within 3 h, whereas the oxidation reaction was not initiated for 8 h when cyclohexene (3 mmol) was added to the same reaction solution.