

Reactions of Co(III)–Nitrosyl Complexes with Superoxide and Their Mechanistic Insights

Pankaj Kumar,[†] Yong-Min Lee,[†] Young Jun Park,[†] Maxime A. Siegler,[‡] Kenneth D. Karlin,^{*,‡} and Wonwoo Nam^{*,†}

[†]Department of Chemistry and Nano Science, Ewha Womans University, Seoul 120-750, Korea

[‡]Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218, United States

S Supporting Information

ABSTRACT: New Co^{III}–nitrosyl complexes bearing N-tetramethylated cyclam (TMC) ligands, [(12-TMC)Co^{III}(NO)]²⁺ (1) and [(13-TMC)Co^{III}(NO)]²⁺ (2), were synthesized via [(TMC)Co^{II}(CH₃CN)]²⁺ + NO(g) reactions. Spectroscopic and structural characterization showed that these compounds bind the nitrosyl moiety in a bent end-on fashion. Complexes 1 and 2 reacted with KO₂/2.2.2-cryptand to produce [(12-TMC)Co^{II}(NO₂)]⁺ (3) and [(13-TMC)Co^{II}(NO₂)]⁺ (4), respectively; these possess O,O'-chelated nitrito ligands. Mechanistic studies using ¹⁸O-labeled superoxide (¹⁸O₂^{•-}) showed that one O atom in the nitrito ligand is derived from superoxide and the O₂ produced comes from the other superoxide O atom. Evidence supporting the formation of a Co–peroxynitrite intermediate is also presented.

Nitric oxide (NO) activation by transition-metal ions has attracted enormous interest from chemists and biochemists since NO has been discovered to play major roles in many biophysiological processes, such as vascular regulation, neurotransmission, and immune cytotoxicity.¹ In this context, the biosynthesis of NO and its various biological and physiological reactivities come about through the interaction with metalloproteins of iron and/or copper.² However, NO overproduction leads to toxicological behavior because of its radical character and ability to form reactive nitrogen species (RNS) such as nitrogen dioxide (NO₂) and peroxynitrite (PN, ⁻OON=O).³ These RNS may result from NO oxidation in the presence of O₂,⁴ H₂O₂, superoxide radical anion (O₂^{•-}),^{3d,5} and/or transition-metal ions.⁶ In these contexts, important enzymes are available in vivo to maintain proper levels of NO. For example, detoxification by removal of NO occurs by nitric oxide dioxygenases, which are microbial or mammalian heme proteins.^{2,7} The chemistry here involves reactions of oxyhemes (e.g., iron(III)–superoxo species) with NO to generate biologically benign nitrate ion, which is believed to occur through the formation of metal–PN intermediates.

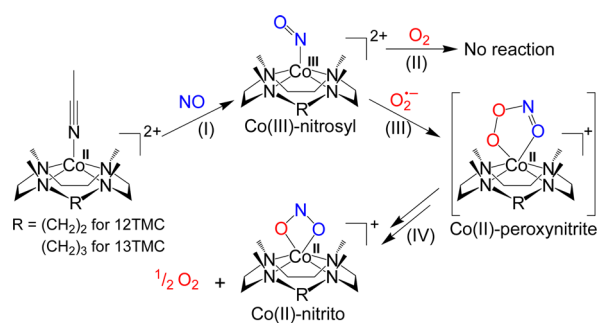
The coordination chemistry of metal–nitrosyl complexes has a long history,^{7b,8} including a significant literature wherein these are exposed to oxidants such as O₂.⁹ Clarkson and Basolo first described the chemistry of a cobalt–nitrosyl complex with O₂, in which oxygenation leads to a nitrite-bound product.^{9a,b} In other examples, a non-heme dinitrosyliron complex reacts with O₂ to give nitrate,^{10a} whereas a copper–NO species gives a Cu–PN

intermediate that transforms to nitrite and O₂.^{10b} Recently, Mondal and co-workers reported the reaction of a Cu–NO complex with H₂O₂ to form a copper–nitrate complex via the thermal decomposition of a presumed Cu^I–PN intermediate.¹¹

Furthermore, there are recent chemistries associated with metal–oxygen coordination complexes with NO. In such biomimetic studies, mononuclear metal–superoxo species have been shown to react with NO to produce metal–PN (Mⁿ⁺–⁻OON=O) intermediates, including examples with heme, non-heme Fe, Co, or Cu.¹² For example, we recently reported the conversion of a non-heme Cr^{IV}–peroxo complex to a Cr^{III}–nitrate ion complex upon addition of NO,^{13a} whereas the reaction of a Cr^{III}–superoxo complex with NO gave a high-valent Cr^{IV}–oxo species and NO₂ via the formation of a presumed Cr^{III}–PN intermediate.^{13b} Thus, a variety of outcomes can occur when metal complexes in varying oxidation states mediate reactions of NO (or NO⁺) with differing reduced O₂ derivatives (e.g., superoxide or peroxide). Included is the capture of a peroxynitrite (or NO₂) intermediate via nitration of added phenols, which is analogous to biologically well-established tyrosine nitration, which effects biomolecule damage or participates in cellular signaling events.^{3a,b,6,14}

Herein we report the synthesis, characterization, and O₂^{•-} reactivity of Co^{III}–nitrosyl complexes bearing 12- and 13-membered N-tetramethylated cyclam (TMC) ligands, [(12-TMC)Co^{III}(NO)]²⁺ (1) (12-TMC = 1,4,7,10-tetramethyl-1,4,7,10-tetraazacyclododecane) and [(13-TMC)Co^{III}(NO)]²⁺ (2) (13-TMC = 1,4,7,10-tetramethyl-1,4,7,10-tetraazacyclotridecane) (Scheme 1, reactions I and III). These Co^{III}–nitrosyl

Scheme 1



Received: December 30, 2014

Published: March 20, 2015

complexes do not react with O_2 (Scheme 1, reaction II) but do react with $O_2^{\bullet-}$ to form the corresponding Co^{II} -nitrito complexes, $[(12-TMC)Co^{II}(NO_2)]^+$ (**3**) and $[(13-TMC)Co^{II}(NO_2)]^+$ (**4**), and O_2 via presumed Co^{II} -PN intermediates (Scheme 1, reactions III and IV). Mechanistic studies using $^{18}O_2^{\bullet-}$ unambiguously showed that one O atom in the nitrito ligand is derived from $O_2^{\bullet-}$ and the other O atom of $O_2^{\bullet-}$ is used to form O_2 (Scheme 1). To the best of our knowledge, this study reports the first mechanistic investigation of the reaction of metal-NO complexes with $O_2^{\bullet-}$ and the first clear evidence showing that O-O bond formation to evolve O_2 occurs in this type of metal-NO oxidative chemistry.

The addition of excess $NO(g)$ to solutions of the cobalt(II) complexes $[(12-TMC)Co^{II}(NCCH_3)]^{2+}$ and $[(13-TMC)Co^{II}(NCCH_3)]^{2+}$ in CH_3CN at $-40^\circ C$ under an Ar atmosphere resulted in the generation of **1** and **2**, respectively, within 1 min (Scheme 1, reaction I; also see the Experimental Section in the Supporting Information (SI); Figure S1 in the SI shows a schematic diagram of the $NO(g)$ purification and handling process). The UV-vis spectra of **1** and **2** exhibit characteristic absorption bands at 368 nm ($\epsilon = 950 M^{-1} cm^{-1}$) and 375 nm ($\epsilon = 750 M^{-1} cm^{-1}$), respectively (Figure 1; also see Figures S2 and

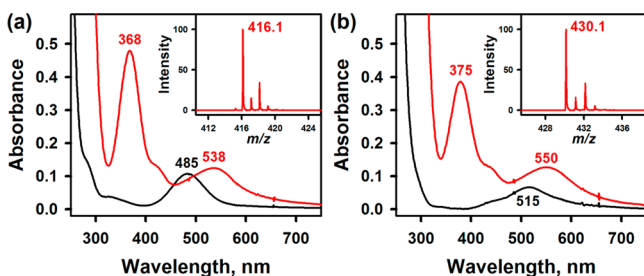


Figure 1. (a) UV-vis spectra of $[(12-TMC)Co^{II}(MeCN)]^{2+}$ (0.50 mM, black line) and **1** (red line). The inset shows the ESI-MS spectrum of **1**. (b) UV-vis spectra of $[(13-TMC)Co^{II}(MeCN)]^{2+}$ (0.50 mM) and **2** (red line). The inset shows the ESI-MS spectrum of **2**.

S3 for the UV-vis spectral changes). Electron paramagnetic resonance (EPR) spectra recorded for **1** and **2** are silent, suggesting the trivalency of the cobalt center (Figure S4; also see Figure S5 for the 1H NMR spectra) and thus formally $Co^{III}(NO^-)$ or $\{Co(NO)\}^8$ descriptions (vide infra).⁸ The solution IR spectra of **1** and **2** are also consistent with these formulations, revealing low-energy (for $\{Co(NO)\}^8$) NO stretching bands at 1712 and 1716 cm^{-1} , respectively (Figures S6 and S7).⁸ Electrospray ionization mass spectrometry (ESI-MS) of **1** and **2** showed prominent ion peaks at m/z 416.1 and 430.1, respectively (Figure 1 insets), whose mass and isotope distribution patterns correspond to $[(12-TMC)Co(NO)(ClO_4)]^+$ (calcd m/z 416.1) and $[(13-TMC)Co(NO)(ClO_4)]^+$ (calcd m/z 430.1) (Figures S8 and S9).

In addition to the above spectroscopic characterization, **1** and **2** were structurally characterized via single-crystal X-ray crystallography. Molecular formulas for the two compounds are $[(12-TMC)Co^{III}(NO)](ClO_4)_2 \{1-(ClO_4)_2\}$ and $[(13-TMC)Co^{III}(NO)](ClO_4)_2 \{2-(ClO_4)_2\}$ (Figure 2 and Tables S1 and S2 in the SI). In both structures, the NO ligand is axially coordinated to the cobalt center in an end-on fashion with a distorted square-pyramidal geometry for cobalt(III), and all four TMC N-methyl groups are oriented syn to the NO moiety. The N(5)-O(1) bond lengths in **1** and **2** are statistically identical (1.155(2) Å in **1** and 1.159(5) Å in **2**). The large bending of the

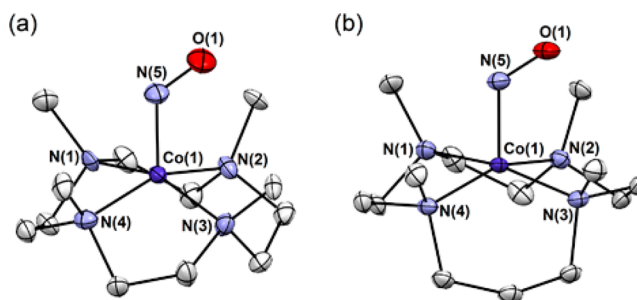


Figure 2. Displacement ellipsoid plots (50% probability level) of (a) $[(12-TMC)Co^{III}(NO)]^{2+}$ (**1**) and (b) $[(13-TMC)Co^{III}(NO)]^{2+}$ (**2**) at 100 K. Disorder and the H atoms have been removed for clarity. Gray, C; blue, N; red, O; dark blue, Co. See Tables S1 and S2 for crystallographic and structural data.

metal-nitrosyl moiety, with $Co(1)-N(5)-O(1)$ bond angles of $128.50(13)^\circ$ for **1** and $124.4(3)^\circ$ for **2**, is also consistent with coordinated NO^- ⁸ and thus is further consistent with our assignment of these complexes as $Co^{III}(NO^-)$ species.

To further elaborate the chemistry of **1** and **2**, we explored their reactions with oxidants, such as O_2 and $O_2^{\bullet-}$. Both Co^{III} -nitrosyl complexes **1** and **2** were found to be inert toward O_2 (Scheme 1, reaction II), in stark contrast to the previously studied cobalt complexes.^{8,9} We speculate that for **1** and **2** there is absolutely no NO dissociation, which may be required for O_2 reactivity.^{7b} However, they do exhibit $O_2^{\bullet-}$ reactivity, as the reaction with KO_2 in CH_3CN with 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (2.2.2-cryptand) gives the corresponding Co^{II} -nitrito complexes (Scheme 1, reactions III and IV). When **1** was reacted with 1 equiv of $O_2^{\bullet-}$ in the presence of 2.2.2-cryptand under an Ar atmosphere in CH_3CN at $-10^\circ C$, the color of the reaction solution changed from dark pink to very light pink (see the Experimental Section in the SI) to form a new species **3**; the characteristic absorption band of **1** at 368 nm disappeared within 2 min (Figures 3 and S10). Similarly, **2** reacted with 1 equiv of $O_2^{\bullet-}$ (Figure S11 shows the UV-vis spectral changes) to form the product **4**. Spectral titration data clearly showed that the stoichiometric ratios for the reactions of both **1** and **2** with $O_2^{\bullet-}$ were 1:1 (Figure S12). The products **3** and **4** obtained in the reactions of $O_2^{\bullet-}$ with **1** and **2**, respectively,

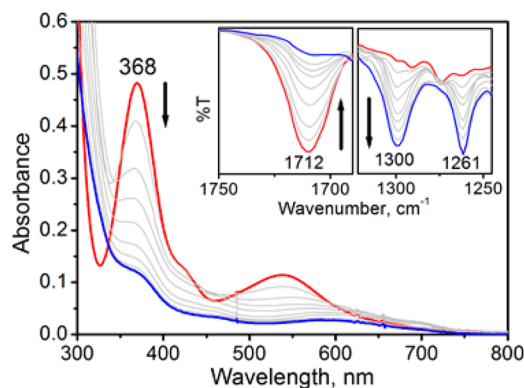


Figure 3. UV-vis spectral changes of **1** (0.50 mM; red line) upon addition of 1 equiv of $KO_2/2.2.2$ -cryptand under an Ar atmosphere in CH_3CN at $-10^\circ C$. The final blue line for **3** was generated within 2 min. The insets show the solution IR spectral changes of **1** (3.0 mM; red lines) upon addition of 1 equiv of $KO_2/2.2.2$ -cryptand under Ar in CH_3CN at $-40^\circ C$. The final blue line for **3** was generated within 0.5 h.

were determined to be Co^{II} -nitrito complexes on the basis of spectroscopic and structural characterization using solution IR and EPR spectroscopy, ESI-MS, and single-crystal X-ray crystallography (vide infra).¹⁵ The yields of **3** and **4** ($85 \pm 4\%$ and $83 \pm 4\%$, respectively) were determined by nitrite ion analyses using either Quantofix test strips or the Griess reagent (see the Experimental Section and Figure S13 in the SI).

The reaction of **1** with 1 equiv of $\text{O}_2^{\bullet-}$ in CH_3CN at -40°C was followed by solution IR spectroscopy (Figure 3 inset). The NO stretching vibration at 1712 cm^{-1} decreased with the simultaneous growth of new peaks at 1261 and 1300 cm^{-1} due to **3**, which are assignable to NO_2^- vibrational signals. Similar spectral changes were observed in the reaction of **2** and $\text{O}_2^{\bullet-}$ (Figure S11a inset), indicating that **4** was generated. The EPR spectra of **3** and **4** exhibit signals at $g = 5.8, 4.3,$ and 2.16 for **3** and $g = 5.9, 3.3,$ and 2.16 for **4**, which are indicative of d^7 high-spin ($S = 3/2$) $\text{Co}(\text{II})$ species (Figure S14a,b).

Absolute confirmation of the Co^{II} -nitrito complexes **3** and **4** was provided by X-ray crystallographic analysis (Figure 4). The

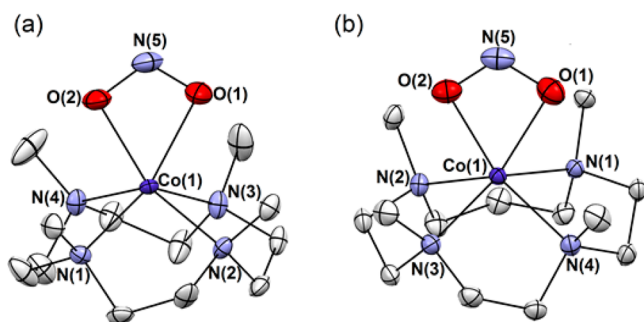


Figure 4. Displacement ellipsoid plots (50% probability level) of (a) $[(12\text{-TMC})\text{Co}^{\text{II}}(\eta^2\text{-O}_2\text{N})]^+$ (**3**) and (b) $[(13\text{-TMC})\text{Co}^{\text{II}}(\eta^2\text{-O}_2\text{N})]^+$ (**4**) at 100 K. H atoms have been omitted for clarity. Gray, C; blue, N; red, O; dark blue, Co. Crystallographic data and selected bond lengths (Å) and angles (deg) for **3** and **4** are summarized in Tables S3 and S4.

complexes $[(12\text{-TMC})\text{Co}^{\text{II}}(\eta^2\text{-O}_2\text{N})]^+$ (**3**) and $[(13\text{-TMC})\text{Co}^{\text{II}}(\eta^2\text{-O}_2\text{N})]^+$ (**4**) possess O,O' -chelated bidentate nitrito ligands, thus giving overall six-coordinate distorted octahedral $\text{Co}(\text{II})$ complexes (see the SI for experimental and structural details; also see Tables S3 and S4). For **3**, there are two crystallographically independent formula units (i.e., $Z' = 2$) with almost identical chemical conformations in the asymmetric unit, whereas $Z' = 1$ for **4**. In both **3** and **4**, the difference of the two $\text{Co}-\text{O}$ bond distances is within 0.02 \AA , reflecting a very minimal Jahn-Teller distortion. This is also consistent with the observed IR spectroscopic properties: the differences between the two $\text{N}-\text{O}$ vibrational signals for **3** and **4** are 39 and 40 cm^{-1} , respectively, which are much smaller than those found in the case of asymmetric binding of NO_2^- to metal centers.¹⁶

ESI-MS was also employed to analyze the source of the oxygen atoms in the NO_2^- ligand for **3** (Figure 5a) and **4** (Figure S15a). The peak at m/z 333.1 in Figure 5a corresponds to $[(12\text{-TMC})\text{Co}(\text{NO}_2)]^+$ (calcd m/z 333.2). We then analyzed **3** prepared using K^{18}O_2 to track the oxygen source in the NO_2^- ligand (see the Experimental Section in the SI); the peak at m/z 335.1 is assigned to $[(12\text{-TMC})\text{Co}^{\text{II}}(\text{N}^{16}\text{O}^{18}\text{O})]^+$ (calcd m/z 335.2) (Figure 5a inset). The observed shift of two mass units from m/z 333.1 to 335.1 indicates that one of the two O atoms in the NO_2^- ligand of **3** is derived from $\text{O}_2^{\bullet-}$ (vide infra).

The supposition that the formation of the Co^{II} -nitrito complex would be accompanied by release of O_2 (Scheme 1,

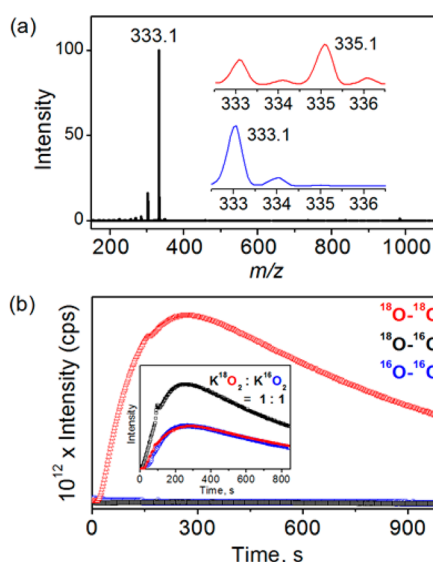
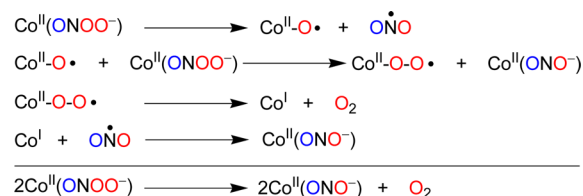


Figure 5. (a) ESI-MS spectrum of **3**. The peak at m/z 333.1 is assigned to $[(12\text{-TMC})\text{Co}^{\text{II}}(\text{NO}_2)]^+$ (calcd m/z 333.2). The insets show the isotope distribution patterns for $3\text{-}^{16}\text{O}^{16}\text{O}$ (blue line) and $3\text{-}^{16}\text{O}^{18}\text{O}$ (red line). (b) Mass spectra of O_2 isotopes produced in the reaction of **1** (2.0 mM) with $\text{K}^{18}\text{O}_2/2.2.2\text{-cryptand}$ (2.0 mM) in CH_3CN at -40°C : $^{16}\text{O}-^{16}\text{O}$, blue circles; $^{16}\text{O}-^{18}\text{O}$, black squares; $^{18}\text{O}-^{18}\text{O}$, red triangles. The inset shows the mass spectra of O_2 isotopes produced using a 1:1 $\text{K}^{16}\text{O}_2/\text{K}^{18}\text{O}_2$ mixture (2.0 mM) to react with **1** (2.0 mM).

reaction IV) comes from both (i) aqueous PN chemistry,^{17,18} where $\text{HOON}=\text{O}$ and $^-\text{OON}=\text{O}$ react to give $2\text{NO}_2^- + \text{O}_2 + \text{H}^+$, and (ii) examples where $\text{Cu}^{\text{II}}\text{-PN}$ complexes were transformed to Cu^{II} -nitrito complexes + O_2 .^{10b,12c,15} Both (i) and (ii) involve the initial formation of PN species, and mechanistic considerations are discussed further below.

As mentioned above, metal-PN complexes may be formed from a variety of reaction types. Here, for the first time, we have described the reaction of a metal-nitrosyl complex with superoxide anion. We propose that in the first step of this reaction, $\text{O}_2^{\bullet-}$ directly adds to the NO moiety in $[(12\text{-TMC})\text{Co}^{\text{III}}(\text{NO})]^{2+}$ (**1**) (or $[(13\text{-TMC})\text{Co}^{\text{III}}(\text{NO})]^{2+}$ (**2**)) to give a transient Co^{II} -PN species that comes about by an internal electron transfer to Co^{III} (Scheme 1, reaction III). Following mechanisms earlier proposed for PN(aq) chemistry involving initial $\text{O}-\text{O}$ homolytic cleavage^{3d} and also applied to $\text{Cu}^{2+}(\text{aq})$ ¹⁵ and nonaqueous copper complex chemistry,^{10b,12c} the sequence of reactions shown in Scheme 2 will lead to the products

Scheme 2



observed (also see Figure S15b for ESI-MS spectra), including a half ^{18}O -labeled nitrite moiety and $^{18}\text{O}_2$. Detection of dioxygen in significant amounts by reaction flask headspace analysis using mass spectrometry (see the Experimental Section in the SI) indeed shows that only $^{18}\text{O}_2$ is formed in the reaction of **1** and $^{18}\text{O}_2^{\bullet-}$ (Figure 5b). This result was confirmed by carrying out a

reaction using a 1:1 $^{16}\text{O}_2^{\bullet-}/^{18}\text{O}_2^{\bullet-}$ mixture, in which a significant amount of $^{16}\text{O}-^{18}\text{O}$ was formed along with $^{16}\text{O}-^{16}\text{O}$ and $^{18}\text{O}-^{18}\text{O}$ (Figure S5 inset). Notably, this finding is exactly consistent with the proposed mechanism in Scheme 2, with initial O–O homolytic cleavage followed by O–O bond formation (Scheme 2, steps 1 and 2).¹⁸ This is the first example in which tracking of the O atoms has revealed that the O_2 produced is derived from the PN peroxidic moiety (here derived from $\text{O}_2^{\bullet-}$), as proposed for aqueous PN chemistry.^{17,18}

While we do not have direct spectroscopic evidence for the postulated $\text{Co}^{\text{II}}-\text{PN}$ species, support for its formation comes from our finding that it can be intercepted by the addition of a phenolic substrate, here 2,4-di-*tert*-butylphenol to produce 2,4-di-*tert*-butyl-6-nitrophenol in good yields (>50%) with oxidative coupling occurring to most of the remaining phenol substrate (see the Experimental Section in the SI). Phenol nitration has been used extensively to provide evidence for the presence of metal–PN species,^{3a,b,6a,14} and as mentioned, this reaction is of considerable biological importance. It is also noted that $\text{Co}-\text{NO}$ complexes **1** and **2** do not react with the phenol.

In summary, we have synthesized two mononuclear $\text{Co}^{\text{III}}-\text{nitrosyl}$ complexes, $[(12\text{-TMC})\text{Co}^{\text{III}}(\text{NO})]^{2+}$ (**1**) and $[(13\text{-TMC})\text{Co}^{\text{III}}(\text{NO})]^{2+}$ (**2**), and examined their reactions with O_2 and $\text{O}_2^{\bullet-}$ (Scheme 1). The $\text{Co}^{\text{III}}-\text{nitrosyl}$ complexes are inert toward O_2 , but for this very new reaction type, they reacted with $\text{O}_2^{\bullet-}$ cleanly to give high yields of $\text{Co}^{\text{II}}-\text{nitrito}$ complexes with the release of O_2 via the formation of presumed $\text{Co}-\text{PN}$ intermediates. It is worth noting that the O_2 evolution involves a rather unique kind of O–O bond-forming process, as otherwise discussed in O_2 -evolving enzymatic reactions such as Photosystem II and chlorite dismutase.¹⁹ The present results add to the very few examples of metal–PN species that form nitrite + O_2 products and provide new mechanistic insights.

■ ASSOCIATED CONTENT

Supporting Information

Experimental section and additional data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Authors

*karlin@jhu.edu

*wwnam@ewha.ac.kr

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the NRF of Korea through CRI (NRF-2012R1A3A2048842 to W.N.) and GRL (NRF-2010-00353 to W.N.), the Research Fellow Program of the MSIP of Korea (NRF-2013R1A1A2061528 to Y.J.P.), and the U.S. National Institutes of Health (to K.D.K.) for support.

■ REFERENCES

(1) (a) Ignarro, J. E. *Nitric Oxide: Biology and Pathobiology*; Academic Press: San Diego, CA, 2000. (b) Richter-Addo, G. B.; Legzdins, P.; Burstyn, J. *Chem. Rev.* **2002**, *102*, 857. (c) Wasser, I. M.; de Vries, S.; Moënnel-Loccoz, P.; Schröder, I.; Karlin, K. D. *Chem. Rev.* **2002**, *102*, 1201. (d) Möller, J. K. S.; Skibsted, L. H. *Chem. Rev.* **2002**, *102*, 1167. (2) (a) Doyle, M. P.; Hoekstra, J. W. *J. Inorg. Biochem.* **1981**, *14*, 351. (b) Cooper, C. E.; Torres, J.; Sharpe, M. A.; Wilson, M. T. *FEBS Lett.* **1997**, *414*, 281. (c) Tocheva, E. I.; Rosell, F. I.; Mauk, A. G.; Murphy, M. E. *P. Science* **2004**, *304*, 867.

(3) (a) Radi, R. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 4003. (b) Kalyanaraman, B. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 11527. (c) Dedon, P. C.; Tannenbaum, S. R. *Arch. Biochem. Biophys.* **2004**, *423*, 12. (d) Goldstein, S.; Lind, J.; Merényi, G. *Chem. Rev.* **2005**, *105*, 2457. (e) Pacher, P.; Beckman, J. S.; Liaudet, L. *Physiol. Rev.* **2007**, *87*, 315. (4) (a) Ford, P. C.; Wink, D. A.; Stanbury, D. M. *FEBS Lett.* **1993**, *326*, 1. (b) Tran, N. G.; Kalyvas, H.; Skodje, K. M.; Hayashi, T.; Moënnel-Loccoz, P.; Callan, P. E.; Shearer, J.; Kirschenbaum, L. J.; Kim, E. *J. Am. Chem. Soc.* **2011**, *133*, 1184. (5) (a) Blough, N. V.; Zafiriou, O. C. *Inorg. Chem.* **1985**, *24*, 3502. (b) Nauser, T.; Koppenol, W. H. *J. Phys. Chem. A* **2002**, *106*, 4084. (6) (a) Qiao, L.; Lu, Y.; Liu, B.; Girault, H. H. *J. Am. Chem. Soc.* **2011**, *133*, 19823. (b) Speelman, A. L.; Lehnert, N. *Acc. Chem. Res.* **2014**, *47*, 1106. (c) Fry, N. L.; Mascharak, P. K. *Acc. Chem. Res.* **2011**, *44*, 289. (7) (a) Gardner, P. R.; Gardner, A. M.; Martin, L. A.; Salzman, A. L. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 10378. (b) Ford, P. C.; Lorkovic, I. M. *Chem. Rev.* **2002**, *102*, 993. (c) Schopfer, M. P.; Mondal, B.; Lee, D.-H.; Sarjeant, A. A. N.; Karlin, K. D. *J. Am. Chem. Soc.* **2009**, *131*, 11304. (8) (a) Enemark, J. H.; Feltham, R. D. *Coord. Chem. Rev.* **1974**, *5*, 686. (b) Richter-Addo, G. B.; Legzdins, P. *Metal Nitrosyls*; Oxford University Press: New York, 1992. (c) McCleverty, J. A. *Chem. Rev.* **2004**, *104*, 403. (d) Berto, T. C.; Speelman, A. L.; Zheng, S.; Lehnert, N. *Coord. Chem. Rev.* **2013**, *257*, 244. (9) (a) Clarkson, S. G.; Basolo, F. J. *J. Chem. Soc. Chem. Commun.* **1972**, *119*, 670. (b) Clarkson, S. G.; Basolo, F. *Inorg. Chem.* **1973**, *12*, 1528. (c) Subedi, H.; Brasch, N. E. *Inorg. Chem.* **2013**, *52*, 11608. (d) Frech, C. M.; Blacque, O.; Schmalle, H. W.; Berke, H. *Dalton Trans.* **2006**, 4590. (10) (a) Skodje, K. M.; Williard, P. G.; Kim, E. *Dalton Trans.* **2012**, *41*, 7849. (b) Park, G. Y.; Deepalatha, S.; Puiiu, S. C.; Lee, D.-H.; Mondal, B.; Narducci Sarjeant, A. A.; del Rio, D.; Pau, M. Y. M.; Solomon, E. I.; Karlin, K. D. *J. Biol. Inorg. Chem.* **2009**, *14*, 1301. (11) Kalita, A.; Kumar, P.; Mondal, B. *Chem. Commun.* **2012**, *48*, 4636. (12) (a) Wick, P. K.; Kissner, R.; Koppenol, W. H. *Helv. Chim. Acta* **2000**, *83*, 748. (b) Roncaroli, F.; Videla, M.; Slep, L. D.; Olabe, J. A. *Coord. Chem. Rev.* **2007**, *251*, 1903. (c) Maiti, D.; Lee, D.-H.; Narducci Sarjeant, A. A.; Pau, M. Y. M.; Solomon, E. I.; Gaoutchenova, K.; Sundermeyer, J.; Karlin, K. D. *J. Am. Chem. Soc.* **2008**, *130*, 6700. (d) Goodwin, J. A.; Coor, J. L.; Kavanagh, D. F.; Sabbagh, M.; Howard, J. W.; Adamec, J. R.; Parmley, D. J.; Tarsis, E. M.; Kurtikyan, T. S.; Hovhannisyann, A. A.; Desrochers, P. J.; Standard, J. M. *Inorg. Chem.* **2008**, *47*, 7852. (e) Kurtikyan, T. S.; Ford, P. C. *Chem. Commun.* **2010**, *46*, 8570. (f) Kurtikyan, T. S.; Eksuzyan, S. R.; Goodwin, J. A.; Hovhannisyann, G. S. *Inorg. Chem.* **2013**, *52*, 12046. (13) (a) Yokoyama, A.; Han, J. E.; Cho, J.; Kubo, M.; Ogura, T.; Siegler, M. A.; Karlin, K. D.; Nam, W. *J. Am. Chem. Soc.* **2012**, *134*, 15269. (b) Yokoyama, A.; Cho, K.-B.; Karlin, K. D.; Nam, W. *J. Am. Chem. Soc.* **2013**, *135*, 14900. (14) Qiao, L.; Lu, Y.; Liu, B.; Girault, H. H. *Metallomics* **2013**, *5*, 686. (15) Babich, O. A.; Gould, E. S. *Res. Chem. Intermed.* **2002**, *28*, 575. (16) Lee, Y.-M.; Oh, M.-J.; Choi, S.-N.; Suh, I.-H.; Lee, J.-H.; Park, J.-R. *Bull. Korean Chem. Soc.* **1998**, *19*, 1382. (17) (a) Pfeiffer, S.; Gorren, A. C. F.; Schmidt, K.; Werner, E. R.; Hansert, B.; Bohle, D. S.; Mayer, B. *J. Biol. Chem.* **1997**, *272*, 3465. (b) Coddington, J. W.; Hurst, J. K.; Lymar, S. V. *J. Am. Chem. Soc.* **1999**, *121*, 2438. (c) Koppenol, W. H.; Bounds, P. L.; Nauser, T.; Kissner, R.; Rügger, H. *Dalton Trans.* **2012**, *41*, 13779. (18) The present formation of $^{16}\text{O}-^{18}\text{O}$ is not consistent with two PN molecules reacting in a “peracid”-type mechanism (but now with two $\text{Co}-\text{PN}$ complexes interacting), where such $\text{PN}(\text{aq})$ solutions give $2\text{NO}_2^- + \text{O}_2$.^{17c} For this “peracid” mechanism, only $^{16}\text{O}_2$ or $^{18}\text{O}_2$ should form when a 1:1 $^{16}\text{O}_2^{\bullet-}/^{18}\text{O}_2^{\bullet-}$ superoxide mixture is used, since molecular oxygen is derived from $^-\text{OO}-\text{NO}_2$ cleavage from an intermediate $\text{PN} (^-\text{OONO}_2)$ species that would form.^{5,17c} (19) (a) Cox, N.; Pantazis, D. A.; Neese, F.; Lubitz, W. *Acc. Chem. Res.* **2013**, *46*, 1588. (b) Rivalta, I.; Brudvig, G. W.; Batista, V. S. *Curr. Opin. Chem. Biol.* **2012**, *16*, 11. (c) Lee, A. Q.; Streit, B. R.; Zdilla, M. J.; Abu-Omar, M. M.; DuBois, J. L. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 15654.