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Reactions of a Chromium(III)-Superoxo Complex and Nitric Oxide That Lead to the Formation of Chromium(IV)-Oxo and Chromium(III)-Nitrito Complexes

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Supporting Information

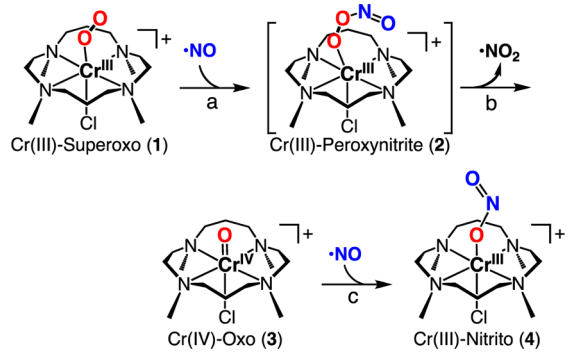
ABSTRACT: The reaction of an end-on Cr(III)-superoxo complex bearing a 14-membered tetraazamacrocyclic TMC ligand, $[Cr^{III}(14\text{-TMC})(O_2)(Cl)]^+$, with nitric oxide (NO) resulted in the generation of a stable Cr(IV)-oxo species, $[Cr^{IV}(14\text{-TMC})(O)(Cl)]^+$, via the formation of a Cr(III)-peroxynitrite intermediate and homolytic O−O bond cleavage of the peroxynitrite ligand. Evidence for the latter comes from electron paramagnetic resonance spectroscopy, computational chemistry and the observation of phenol nitration chemistry. The Cr(IV)-oxo complex does not react with nitrogen dioxide (NO_2), but reacts with NO to afford a Cr(III)-nitrito complex, $[Cr^{III}(14\text{-TMC})(NO_2)(Cl)]^+$. The Cr(IV)-oxo and Cr-(III)-nitrito complexes were also characterized spectroscopically and/or structurally.

Nitric oxide (NO) is a ubiquitous signal transduction molecule found in a wide variety of physiological processes, such as in cellular signaling leading to smooth muscle vasodilation, platelet disaggregation, and neurotransmission and in the immune response to bacterial infection.[1] However, NO itself is a toxin because of the reactivity derived from its radical character and ability to form more reactive and deleterious oxidation products, such as nitrogen dioxide (NO_2) and peroxynitrite (PN, oxoperoxonitrate(−), $^-OON{=}O$), in the presence of transition metals.[2] In this context, various life forms have constructed detoxification systems: widely occurring nitric oxide dioxygenases (NODs) are enzymes that catalyze the conversion of toxic NO to biologically atoxic nitrate (NO_3^-) with NAD(P)H (i.e., $2NO + 2O_2 + NAD(P)H \rightarrow 2NO_3^- + NAD(P)^+ + H^+$).[3] In NOD reactions, including those observed with hemoglobins and myoglobins, an Fe(III)-superoxo species ($Fe^{III}(O_2^{\bullet-})$), which is generated in the reaction of Fe(II) + O_2, reacts with NO to yield NO_3^- via formation of an Fe^{III}-PN intermediate.[4,5] Here, a ferryl species ($Fe^{IV}(O)$) is proposed to be formed via homolytic O−O bond cleavage of the Fe^{III}-PN species; Groves et al. only very recently provided time-resolved spectrophotometric evidence for the formation of such a ferryl species in the reaction of myoglobin with PN.[6] However, a heme-PN moiety has not been detected due to its expected short lifetime and rapid recombination with NO_2 in a $[Fe^{IV}{=}O\ {}^{\bullet}NO_2]$ cage to give a NO_3^- product. Thus, the study of metal-superoxo intermediates with NO is of great interest with regard to the investigation of reaction pathways or undetected intermediate reactivity, such as in the possible escape of a bound PN or NO_2 molecule.[7]

Recently, *N*-tetramethylated cyclam[8] (TMC)-chelated redox-active first-row transition metal complexes and their peroxo (O_2^{2-}) and superoxo ($O_2^{\bullet-}$) derivatives have been systematically synthesized and investigated in various oxidation reactions.[9−12] In the cases of Ni and Cr complexes with 14-TMC and 12-TMC ligands,[13] the TMC ring size was found to alter the structure of the resulting $[M(n\text{-TMC})(O_2)]^{n+}$ complexes; the larger ring size ligand (e.g., 14-TMC) forms metal-superoxo complexes (e.g., Ni^{II}-$O_2^{\bullet-}$ [10b] and Cr^{III}-$O_2^{\bullet-}$ [11]), whereas the smaller ring size 12-TMC chelate forms metal-peroxo complexes (e.g., Ni^{III}-O_2^{2-} [10b] and Cr^{IV}-O_2^{2-} [12]). In addition, we recently reported the NOD reactivity of the Cr^{IV}-peroxo complex: this species reacted with NO to give a Cr(III)-nitrate product, $[Cr^{III}(12\text{-TMC})(NO_3)(Cl)]^+$, but no intermediates such as Cr-PN or Cr-oxo species were detected.[12]

We herein report the reactions of the end-on Cr^{III}-$O_2^{\bullet-}$ complex bearing the 14-TMC ligand, $[Cr^{III}(14\text{-TMC})(O_2)(Cl)]^+$ (**1**), with NO. Reaction of complex **1** with 1 equiv of NO generates a stable Cr(IV)-oxo species, $[Cr^{IV}(14\text{-TMC})(O)(Cl)]^+$ (**3**), via the formation of a presumed Cr^{III}-PN intermediate, $[Cr^{III}(14\text{-TMC})(OON{=}O)(Cl)]^+$ (**2**) (Scheme 1, reactions a and b), unlike the NO reaction of a Cr^{IV}-O_2^{2-}

Scheme 1



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complex bearing 12-TMC.[12] To the best of our knowledge, this study presents the first strong evidence for the formation of a high-valent metal-oxo complex in the reaction of a metal-superoxo species and NO. Further, **3** does not lead to a NO_3^--containing product with NO_2 addition, but it does react with NO to give a Cr(III)-nitrito complex, $[Cr^{III}(14\text{-TMC})(NO_2)(Cl)]^+$ (**4**) (Scheme 1, reaction c). Thus, we were able to follow all the reaction pathways of metal−oxygen intermediates with NO, employing isolated or spectroscopically well-characterized Cr complexes.

The starting chromium complex, $[Cr^{II}(14\text{-TMC})(Cl)]Cl$, was synthesized according to literature methods, and the Cr^{III}-$O_2^{\bullet-}$ complex (**1**, 2 mM) was prepared by bubbling O_2 for 30 s in an CH_3CN solution containing the starting complex at −40 °C, giving a dark red color.[11] After the reaction solution was purged with Ar for 30 min at −40 °C, 1 equiv of NO[14] was added, and the mixture was stirred for 20 min (see Supporting Information (SI), Figure S1, for a schematic diagram showing the NO purification setup), whereupon the color of the solution changed from red to yellowish green (see Figure 1 for the UV/vis spectral changes). In

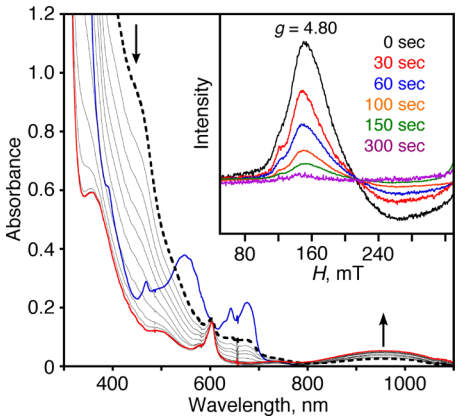

Figure 1. Changes in the UV/vis spectrum **1** (2 mM) upon addition of 1 equiv of NO in CH_3CN at −40 °C under Ar. The initial blue solid line spectrum (**1**) changed immediately to the black dashed line spectrum (**2**) upon addition of NO, followed by the conversion to the red solid line spectrum (**3**) over 15 min. Inset: time-dependent EPR spectra of Cr^{III}-PN intermediate (**2**) in CH_3CN at 5 K. **1** and NO were mixed in CH_3CN at −40 °C under Ar, and EPR spectra were obtained from such frozen solutions as a function of time (0, 30, 60, 100, 150, and 300 s).

this experiment, the spectrum of **1** changed from the blue solid line to the black dashed line immediately upon addition of NO, followed by conversion of this intermediate (**2**) to the Cr^{IV}-oxo species (**3**, red line) with λ_{max} = 603 nm (80 M^{-1} cm^{-1}) over 15 min (Figure 1). This final absorption spectrum is consistent with our previous report on the Cr^{IV}-oxo complex with 14-TMC,[11] and the conversion of **1** to **3** turned out to be quantitative. A resonance Raman spectrum of **3** was collected using 407-nm excitation in CH_3CN at −20 °C (Figure S2). The peak observed at 874 cm^{-1} is comparable to the Cr−O frequency (873 cm^{-1}) of the previously reported $[Cr^{IV}(14\text{-TMC})(O)(Cl)]^+$ complex.[11] The electrospray ionization mass spectrum (ESI-MS) of **3** also supports the generation of Cr^{IV}-oxo species; the observed peak cluster centered at m/z 359.3 can be assigned to a Cr^{IV}-oxo complex formulated as $[Cr^{IV}(14\text{-TMC})(O)(Cl)]^+$ (calcd m/z 359.2) (Figure S3). An electron paramagnetic resonance (EPR) spectrum obtained for **3** (1 mM) in CH_3CN at 5 K was silent, consistent with the expected oxidation state of Cr^{IV} in **3**. Based on the spectroscopic characterization of **3**, we were able to conclude unambiguously that a high-valent Cr^{IV}-oxo species was formed in the reaction of this Cr^{III}-$O_2^{\bullet-}$ complex and NO.

A proposed mechanism for the generation of a Cr^{IV}-oxo species (**3**) in the reaction of Cr^{III}-$O_2^{\bullet-}$ (**1**) and NO is depicted in Scheme 1. According to widely accepted discussions on the reaction mechanism of Fe^{III}-$O_2^{\bullet-}$ species with NO,[2−6] the first step must be a radical-coupling reaction between **1** and NO to generate the Cr^{III}-PN intermediate, $[Cr^{III}(14\text{-TMC})(OON{=}O)(Cl)]^+$ (**2**) (Scheme 1, reaction a). This species gives rise to **3** and NO_2 via O−O bond homolysis of the PN ligand (Scheme 1, reaction b). The Cr^{IV}-oxo species generated does not react further with the NO_2 produced simultaneously, unlike the case for NOD reactions,[3−6] and it maintains its metal-oxo structure under the reaction conditions.

We then attempted to characterize the presumed Cr^{III}-PN intermediate (**2**) and elucidate the mechanism of its conversion to the Cr^{IV}-oxo species (**3**) (Scheme 1, reaction b). First, the UV/vis spectrum shown as a black dashed line in Figure 1 likely represents that of **2**. Notably, the dashed line spectrum and the following changes shown in Figure 1 were not observed when the reaction was carried out at higher temperatures (e.g., 0 °C). For this latter experiment, the spectrum changed instantly from the blue solid line (**1**) to the red line (**3**) without showing any intermediate spectra, implying that the stability of **2** depends on the reaction temperature and **2** is detectable only at low temperature. We also found via EPR measurements that the intermediate species (i.e., the black dashed line in Figure 1) exhibited a signal assignable to a d^3 Cr(III) ion (S = 3/2) at 5 K (Figure S4a),[15] while complexes **1** and **3** were EPR-silent. Moreover, time-dependent EPR measurements revealed the clear conversion of **2** to **3**: EPR spectra in CH_3CN at 5 K obtained by freezing solutions of the **1** + NO reaction mixture as a function of time (0−300 s) indicated that the signal intensity decreased as time passed, leading from EPR-active **2** to EPR-silent **3** (Figure 1, inset). Thus, the Cr(III) EPR signal detected for **2** supports the generation of a Cr^{III}-PN species, which decomposes to the EPR-silent species **3**.[16] As reported previously, the lifetimes of metal-peroxynitrite species are very short for species generated near room temperature.[17] A striking recent success is a Co^{III}-PN porphyrinate complex, yet still generated under cryogenic conditions, but thoroughly characterized by using IR spectroscopy and isotope labeling experiments along with density functional theory (DFT) calculations.[18]

DFT calculations were also performed to further support our suppositions concerning the intermediacy of Cr^{III}-PN complex **2**. Complex **1** is an S = 1 state species,[9a,11b] but upon addition of the NO spin (up or down), the whole system can reside in two energetically degenerate states, S = 1/2 or 3/2. The calculations reveal that the S = 1/2 state features a concerted high-energy barrier for the current reaction (Figure 2), and it is therefore not discussed further.[19] The S = 3/2 state reaction pathway is shown to be able to proceed in two low-energy steps. The first step occurs over a low barrier of 1.7 kcal/mol, such that a very fast reaction of **1** with NO would occur, and alternative reactions are unlikely. Moreover, the product is the stable O-bound PN species **2** at −10.8 kcal/mol (Figure S5). The second step occurs over a barrier of 20.1 kcal/mol to form the Cr^{IV}-oxo complex **3**. This barrier is somewhat high, but it is likely overestimated.[20] All in all, the interpretation of the calculations strongly supports that the formation of the S = 3/2 species **2** is likely, and its transformation to **3** is quite possible.

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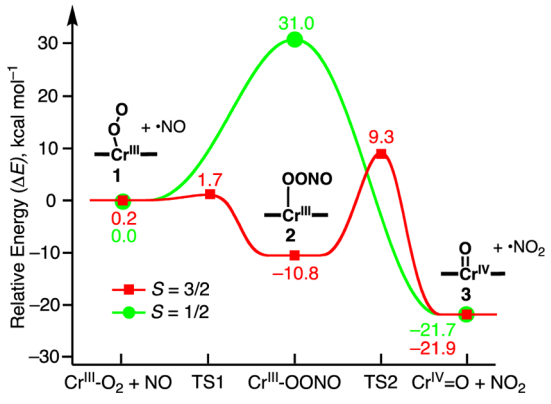
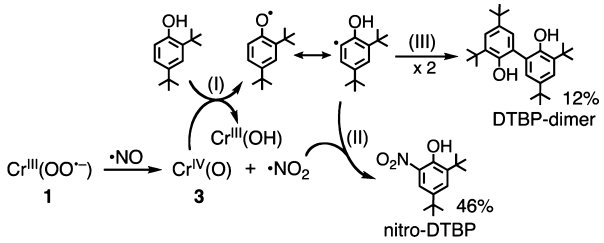


Figure 2. DFT-calculated pathways for the reaction of $[Cr^{III}(14\text{-TMC})(O_2)(Cl)]^+$ (**1**) with NO. The low-energy two-step pathway giving PN complex **2** and then Cr^{IV}=O species **3** occurs on the $S = 3/2$ surface (red, ■), while the $S = 1/2$ surface (green, ●) exhibits a concerted pathway that does not feature a (stable) peroxynitrite intermediate (**2**).

We sought more support for our mechanistic proposal, including the formation of **3** from **2** with the liberation of NO_2. In this regard, we carried out trapping experiments using 2,4-di-*tert*-butylphenol (DTBP) to obtain evidence that NO_2 is produced concomitantly with the Cr^{IV}-oxo formation (Scheme 1, reaction b).[22] After the generation of **3** as discussed above, 1 equiv of DTBP was added to the resulting solution, which was then stirred for 20 min under Ar, while the reaction's UV/vis spectral changes were monitored (see Figure S6). ESI-MS analysis of the resulting solution revealed the presence of a Cr^{III}-hydroxo species at m/z 360.2 ($[Cr^{III}(14\text{-TMC})(OH)(Cl)]^+$, calcd m/z 360.3; Figure S6). Further product analysis was performed using GC and ^{1}H NMR spectroscopic measurements. Nitrated DTBP (2,4-di-*tert*-butyl-6-nitrophenol, nitro-DTBP) and oxidatively dimerized DTBP (2,2′-dihydroxy-3,3′,5,5′-tetra-*tert*-butylbiphenol, DTBP-dimer) were produced in 46% and 12% yields, respectively (see SI for experimental details). The results can be readily explained as follows: First, H-atom abstraction reaction of DTBP by **3** gives a phenoxyl radical and a Cr^{III}-hydroxo complex (Scheme 2,

Scheme 2



reaction I). The phenoxyl radical traps gaseous NO_2 to give nitro-DTBP (Scheme 2, reaction II) or dimerizes to give DTBP-dimer (Scheme 2, reaction III). Thus, the fact that we successfully trapped and recovered NO_2 in good yield strongly supports the proposed reaction mechanism involving the formation of a Cr^{IV}-oxo complex and NO_2 via homolytic O−O bond cleavage of a Cr^{III}-PN intermediate (Scheme 1, reaction b).

In heme and non-heme systems, the reaction of a ferryl species and NO has been of great interest in terms, for example, of the inhibition of cytochrome *bd* oxidase reactivity.[23] Here, a ferryl heme species reacts with NO to generate a ferric species and nitrite (Fe^{III} + NO_2^-),[23,24] while a ferryl non-heme complex ($[Fe^{IV}(14\text{-TMC})(O)(OAc)]^+$) with added NO produces a ferrous species and nitrite (Fe^{II} + NO_2^-).[25] The reactions of other metal-oxo complexes and NO have also been discussed.[26] Since we did not observe NO_3^- formation via a coupling between the Cr^{IV}-oxo complex **3** and NO_2 (*vide supra*) and the formation of a Cr^{III}-nitrito complex, $[Cr^{III}(14\text{-TMC})(NO_2)(Cl)]^+$ (**4**), was observed when an excess amount of NO was used in the reaction of Cr^{III}-$O_2^{\bullet-}$ complex **1**, we decided to check if **3** could react with NO, not with NO_2, to form **4** (Scheme 1, reaction c). Indeed, this is the case. After **3** was generated as described above, the solution was degassed by Ar bubbling to remove NO_2 (*vide supra*), and then excess NO was added over the top of the solution at −40 °C. The UV/vis spectral changes upon addition of NO and the ESI-MS of the resulting solution are depicted in Figure 3; the

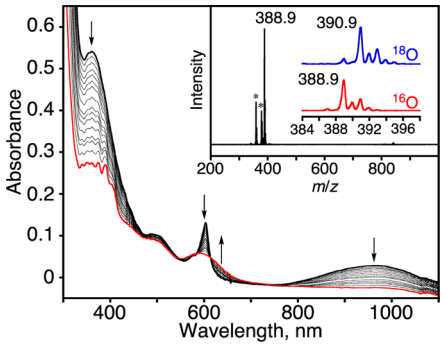


Figure 3. Changes in the UV/vis spectrum of **3** (black line) upon addition of NO (10 cm^3) into the headspace above a solution of **3** in CH_3CN at −40 °C under Ar. Inset: ESI-MS spectrum of $[Cr^{III}(14\text{-TMC})(NO_2)(Cl)]^+$ (**4**) (calcd m/z 389.1) and isotope distribution patterns for **4**-^{16}O (red) and **4**-^{18}O (blue). The peaks at m/z 359.1 and 378.1 marked with asterisks are assigned to $[Cr^{IV}(14\text{-TMC})(O)(Cl)]^+$ (calcd m/z 359.2) and $[Cr^{III}(14\text{-TMC})(Cl_2)]^+$ (calcd m/z 378.1), respectively.

characteristic absorption band of **3** at 603 nm disappeared gradually over 5 min, and a molecular ion peak corresponding to **4** appeared at m/z 388.9. When **1** was prepared with isotopically labeled $^{18}O_2$ and used in the subsequent reaction with NO, a peak corresponding to $[Cr^{III}(14\text{-TMC})(N^{18}O^{16}O)(Cl)]^+$ (calcd m/z 391.2) was found at m/z 390.9 (Figure 3, inset). The 2-mass-unit shift observed upon substitution of ^{16}O with ^{18}O indicates that **4** has one ^{18}O oxygen (out of two) in it and its origin is the Cr^{III}-$O_2^{\bullet-}$ complex **1** via Cr^{IV}-oxo species **3** (Scheme 1, reaction c). Additionally, an EPR spectrum of **4** in CH_3CN at 5 K showed a signal assigned to a d^3 Cr(III) ion ($S = 3/2$)[15] (Figure S3b). Based on the results presented above, we conclude that one-electron reduction of Cr occurs through the reaction between **3** and NO, resulting in the formation of $[Cr^{III}(14\text{-TMC})(NO_2)(Cl)]^+$ (**4**; see Figure S6).

In summary, we have demonstrated the generation of a stable Cr(IV)-oxo species (**3**) in the reaction of a Cr(III)-superoxo complex (**1**) and nitric oxide. This is the first clear observation of metal-oxo species generation in the reaction of a metal-superoxo complex and NO via metal-peroxynitrite formation and subsequent homolytic O−O bond cleavage. This opens the way to utilize such an approach to generate biochemical or synthetic higher-valent metal-oxo species. Interestingly, the Cr(IV)-oxo species did not show any reactivity toward NO_2, unlike NOD reactions, but it readily reacted with NO to form a Cr(III)-nitrito complex (**4**). In addition, we have shown that the

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ring size of the TMC ligand has a significant effect not only on the determination of metal-O_2 structures but also on the reactivity of the resulting metal-oxo complexes toward NO and NO_2.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details, purification of NO, trapping experiments, spectroscopic and kinetic data, and DFT calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Ignarro, J. E. *Nitric Oxide, Biology and Pathobiology*; Academic Press: San Diego, CA, 2000. (b) Wasser, I. M.; de Vries, S.; Moënne-Loccoz, P.; Schröder, I.; Karlin, K. D. *Chem. Rev.* **2002**, *102*, 1201. (c) Møller, J. K. S.; Skibsted, L. H. *Chem. Rev.* **2002**, *102*, 1167. (d) Richter-Addo, G. B.; Legzdins, P.; Burstyn, J. *Chem. Rev.* **2002**, *102*, 857. (e) Toledo, J. C., Jr.; Augusto, O. *Chem. Res. Toxicol.* **2012**, *25*, 975.

(2) (a) Ford, P. C.; Fernandez, B. O.; Lim, M. D. *Chem. Rev.* **2005**, *105*, 2439. (b) Schopfer, M. P.; Wang, J.; Karlin, K. D. *Inorg. Chem.* **2010**, *49*, 6267. (c) Fry, N. L.; Mascharak, P. K. *Acc. Chem. Res.* **2011**, *44*, 289. (d) Heilman, B. J.; St. John, J.; Oliver, S. R. J.; Mascharak, P. K. *J. Am. Chem. Soc.* **2012**, *134*, 11573. (e) Berto, T. C.; Speelman, A. L.; Zheng, S.; Lehnert, N. *Coord. Chem. Rev.* **2013**, *257*, 244. (f) Xu, N.; Goodrich, L. E.; Lehnert, N.; Powell, D. R.; Richter-Addo, G. B. *Angew. Chem., Int. Ed.* **2013**, *52*, 3896. (g) Martirosyan, G. G.; Kurtikyan, T. S.; Azizyan, A. S.; Iretskii, A. V.; Ford, P. C. *J. Inorg. Biochem.* **2013**, *121*, 129.

(3) (a) Doyle, M. P.; Hoekstra, J. W. *J. Inorg. Biochem.* **1981**, *14*, 351. (b) Eich, R. F.; Li, T.; Lemon, D. D.; Doherty, D. H.; Curry, S. R.; Aitken, J. F.; Mathews, A. J.; Johnson, K. A.; Smith, R. D.; Phillips, G. N., Jr.; Olsen, J. S. *Biochemistry* **1996**, *35*, 6976. (c) Gardner, P. R.; Gardner, A. M.; Martin, L. A.; Salzman, A. L. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 10378.

(4) (a) Ouellet, H.; Ouellet, Y.; Richard, C.; Labarre, M.; Wittenberg, B.; Wittenberg, J.; Guertin, M. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 5902. (b) Gardner, P. R. *J. Inorg. Biochem.* **2005**, *99*, 247.

(5) (a) Mehl, M.; Daiber, A.; Herold, S.; Shoun, H.; Ullrich, V. *Nitric Oxide* **1999**, *3*, 142. (b) Ferrer-Sueta, G.; Radi, R. *ACS Chem. Biol.* **2009**, *4*, 161. (c) Perrin, D.; Koppenol, W. H. *Arch. Biochem. Biophys.* **2000**, *377*, 266.

(6) Su, J.; Groves, J. T. *Inorg. Chem.* **2010**, *49*, 6317.

(7) (a) Schopfer, M. P.; Mondal, B.; Lee, D.-H.; Narducci Sarjeant, A. A.; Karlin, K. D. *J. Am. Chem. Soc.* **2009**, *131*, 11304. (b) Park, G. Y.; Deepalatha, S.; Puiu, 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. (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) Herold, S.; Koppenol, W. H. *Coord. Chem. Rev.* **2005**, *249*, 499. (e) Pestovsky, O.; Bakac, A. *J. Am. Chem. Soc.* **2002**, *124*, 1698.

(8) Barefield, E. K. *Coord. Chem. Rev.* **2010**, *254*, 1607.

(9) (a) Cho, J.; Sarangi, R.; Nam, W. *Acc. Chem. Res.* **2012**, *45*, 1321. (b) Cho, J.; Jeon, S.; Wilson, S. A.; Liu, L. V.; Kang, E. A.; Braymer, J. J.; Lim, M. H.; Hedman, B.; Hodgson, K. O.; Valentine, J. S.; Solomon, E. I.; Nam, W. *Nature* **2011**, *478*, 502.

(10) (a) Kieber-Emmons, M. T.; Annaraj, J.; Seo, M. S.; Van Heuvelen, K. M.; Tosha, T.; Kitagawa, T.; Brunold, T. C.; Nam, W.; Riordan, C. G. *J. Am. Chem. Soc.* **2006**, *128*, 14230. (b) Cho, J.; Sarangi, R.; Annaraj, J.; Kim, S. Y.; Kubo, M.; Ogura, T.; Solomon, E. I.; Nam, W. *Nature Chem.* **2009**, *1*, 568.

(11) (a) Cho, J.; Woo, J.; Nam, W. *J. Am. Chem. Soc.* **2010**, *132*, 5958. (b) Cho, J.; Woo, J.; Nam, W. *J. Am. Chem. Soc.* **2012**, *134*, 11112.

(12) 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.

(13) Abbreviations used: 12-TMC, 1,4,7,10-tetramethyl-1,4,7,10-tetraazacyclododecane; 14-TMC, 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane.

(14) A NO-saturated solution was prepared under 1 atm at 298 K; the concentration of the NO in CH_3CN at 293 K was approximated to be 14 mM. For the published values for NO solubilities in organic solvents, see: Young, C. L *Oxides of Nitrogen*; Solubility Data Series Vol. *8*; International Union of Pure and Applied Chemistry: 1981. The purification of NO is described in the SI (experimental section and Figure S1).

(15) (a) Hempel, J. C.; Morgan, L. O.; Lewis, W. B. *Inorg. Chem.* **1970**, *9*, 2064. (b) Ueki, S.; Yamauchi, J. *Inorg. Chim. Acta* **2002**, *338*, 13.

(16) Characterization of the Cr^{III}-PN species **2** with ESI-MS in this case was unsuccessful due to its thermal instability. We note that there is no example of resonance Raman spectroscopic characterization of a metal-peroxynitrite complex, probably due to photodecay of the intermediate during measurements: Tran, N. G.; Kalyvas, H.; Skodje, K. M.; Hayashi, T.; Moënne-Loccoz, P.; Callan, P. E.; Shearer, J.; Kirschenbaum, L. J.; Kim, E. *J. Am. Chem. Soc.* **2011**, *133*, 1184.

(17) (a) Goldstein, S.; Lind, J.; Merényi, G. *Chem. Rev.* **2005**, *105*, 2457. (b) Yukl, E. T.; de Vries, S.; Moënne-Loccoz, P. *J. Am. Chem. Soc.* **2009**, *131*, 7234. (c) Kurtikyan, T. S.; Ford, P. C. *Chem. Commun.* **2010**, *46*, 8570.

(18) (a) Kurtikyan, T. S.; Eksuzyan, S. R.; Hayrapetyan, V. A.; Martirosyan, G. G.; Hovhannisyan, G. S.; Goodwin, J. A. *J. Am. Chem. Soc.* **2012**, *134*, 13861. (b) Wick, P. K.; Kissner, R.; Koppenol, W. H. *Helv. Chim. Acta* **2000**, *83*, 748.

(19) This would correspond to a reaction where the added NO abstracts an O-atom from the superoxo complex to directly produce NO_2.

(20) Inclusion of entropy and other correction factors, even though this process includes a formal error (see SI, DFT methods),[21] gives an estimated barrier of 16.7 kcal/mol (see Table S1). In addition, dissociation entropy of NO_2 is expected to stabilize the products even more than what is calculated, thereby indirectly further lowering the transition state.

(21) Ho, J.; Klamt, A.; Coote, M. L. *J. Phys. Chem. A* **2010**, *114*, 13442.

(22) (a) Coombes, R. G.; Diggle, A. W. *Tetrahedron Lett.* **1993**, *34*, 8557. (b) Coombes, R. G.; Diggle, A. W. *Tetrahedron Lett.* **1994**, *35*, 6373. (c) Geletii, Y. V.; Patel, A. D.; Hill, C. L.; Casella, L.; Monzani, E. *React. Kinet. Catal. Lett.* **2002**, *77*, 277. (d) Ischiropoulos, H.; Zhu, L.; Chen, J.; Tsai, M.; Martin, J. C.; Smith, C. D.; Beckman, J. S. *Arch. Biochem. Biophys.* **1992**, *298*, 431. (e) Geletti, Y. V.; Bailey, A. J.; Boring, E. A.; Hill, C. L. *Chem. Commun.* **2001**, 1484.

(23) Borisov, V. B.; Forte, E.; Sarti, P.; Brunori, M.; Konstantinov, A. A.; Giuffrè, A. *FEBS Lett.* **2006**, *580*, 4823.

(24) Herold, S.; Rehmann, F.-J. K. *J. Biol. Inorg. Chem.* **2001**, *6*, 543.

(25) Owen, T. M.; Rohde, J.-U. *Inorg. Chem.* **2011**, *50*, 5283.

(26) (a) De Leo, M.; Ford, P. C. *J. Am. Chem. Soc.* **1999**, *121*, 1980. (b) Nemes, A.; Pestovsky, O.; Bakac, A. *J. Am. Chem. Soc.* **2002**, *124*, 421. (c) Man, W.-L.; Lam, W. W. Y.; Ng, S.-M.; Tsang, W. Y. K.; Lau, T.-C. *Chem.—Eur. J.* **2012**, *18*, 138.