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NO_2^- Activation and Reduction to NO by a Nonheme $Fe(NO_2)_2$ Complex

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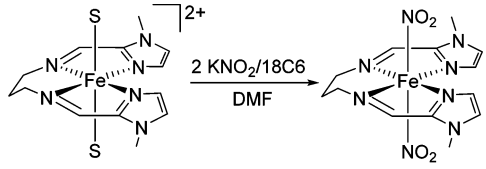
Supporting Information

ABSTRACT: The selective reduction of nitrite (NO_2^-) to nitric oxide (NO) is a fundamentally important chemical transformation related to environmental remediation of NO_x and mammalian blood flow. We report the synthesis and characterization of two nonheme Fe complexes, $[Fe(LN_4^{Im})(MeCN)_2](BF_4)_2$ ($\mathbf{1}^{MeCN}$) and $[Fe(LN_4^{Im})(NO_2)_2]$ (**2**), geared toward understanding the NO_2^- to NO conversion. Complex **2** represents the first structurally characterized Fe^{II} complex with two axial NO_2^- ligands that functions as a nitrite reduction catalyst.

While the physiological properties of nitric oxide (NO) have been established over the past four decades,[1] several other small inorganic molecules have emerged that exhibit important biological activities. This list includes reactive nitrogen species (RNS) such as nitrite (NO_2^-)[2] and nitroxyl (HNO)[3] and S-containing molecules such as hydrogen sulfide (H_2S).[4] In particular, the biochemical properties of NO_2^- have been the focus of recent research efforts, which stems from its role in the global nitrogen cycle and its potential therapeutic use in diseases related to blood flow.[2] For example, the overuse of nitrogen-rich fertilizers has led to an increase in nitrate (NO_3^-) and NO_2^- concentrations to toxic levels in water runoff.[5] Thus, removal of these nitrogen oxides by denitrifying bacteria or synthetic catalysts is a key process in municipal water treatment.[6] Additionally, in vivo vascular levels of NO_2^- approach high μM concentrations where it serves as an emergency storage pool of NO.[7] The two-proton, one-electron reduction of NO_2^- to NO is effectively carried out in microbes by nitrite reductase enzymes (NiR: $NO_2^- + 2H^+ + e^- \rightarrow NO + H_2O$) utilizing type 2 Cu or heme-Fe (cd_1) cofactors.[2c] Although no such human NiR exists, several heme proteins have demonstrated NiR activity under hypoxic conditions.[2] These studies emphasize nitrite's role as an alternative (nitric oxide synthase (NOS) independent) reservoir of NO during times of stress. Indeed, this activity has been observed in several mammalian proteins including deoxyhemoglobin, endothelial NOS, and cytochrome *c* oxidase.[2a] This property emphasizes the significant role Fe-containing proteins play in the physiological equilibrium between NO_2^- and NO.

Due to the environmental and physiological importance of the NO_2^- to NO conversion, several groups have pursued synthetic analogues of NiRs.[9,10] Examples of functional Cu-NiR[8,9] analogues are greater than their Fe counterparts.[10] This absence is because of the tendency to form Fe reaction byproducts that halt the catalytic cycle including oxo-bridged $Fe^{III}-O-Fe^{III}$ and "inert" $\{FeNO\}^7$ derivatives.[10] Encouraged by our findings in nonheme-mediated reduction of NO with pyrrole ligands, we transitioned to the design of NO_2^- reduction catalysts.[11] We thus synthesized a planar, neutral, imine/imidazole, N_4-ligand (LN_4^{Im}) to permit the binding of NO_2^- ligands in vacant or solvent-bound axial positions (Scheme 1). We hypothesized that the decreased basicity of

Scheme 1. Synthesis of 2 (S = solvent ligands)



LN_4^{Im} would circumvent the formation of stable $\{FeNO\}^7$ products and facilitate catalytic reduction of NO_2^-. Herein, we report the synthesis, structure, and properties of $[Fe(LN_4^{Im})(MeCN)_2](BF_4)_2$ ($\mathbf{1}^{MeCN}$) and $[Fe(LN_4^{Im})(NO_2)_2]$ (**2**) (Scheme 1). To our knowledge, **2** is the first example of a nonheme $Fe^{II}-(NO_2)_2$ complex that exhibits catalytic NiR activity.

Complex $\mathbf{1}^{MeCN}$ was synthesized by treating an MeCN solution of LN_4^{Im} with $[Fe(H_2O)_6](BF_4)_2$ (1:1) affording the red Fe^{II} complex (λ_{max}: 478 nm in MeCN, Figure S4 in the Supporting Information = SI) in 92% yield. Complex $\mathbf{1}^{MeCN}$ has been characterized by various spectroscopies and X-ray diffraction (Figure 1) to support its formulation (see the SI). Complex **1** reacted readily with KNO_2 (1:2, solubilized with 18-crown-6 ether = 18C6) in DMF to result in precipitation of the violet N-bound (nitro) species **2** in 85% yield (Scheme 1). Spectroscopic features in the UV–vis (λ_{max}: 574 nm in MeCN, Figure S4) and FTIR (^{15}N-senstive peaks at 1327, 1281, and 813 cm^{-1}, KBr, Figure S3)[12] are consistent with its formation. The isolation of **2** from stoichiometric addition of NO_2^- is noteworthy as reacting an Fe^{II}–P (where P = porphyrin) complex with excess NO_2^- only results in the mononitro derivative.[13] This observation has been attributed to the strong π-accepting ability of NO_2^- and is exemplified by the low-spin (LS) nature of Fe in the $Fe-P-NO_2$ complex. Complex **2** is no

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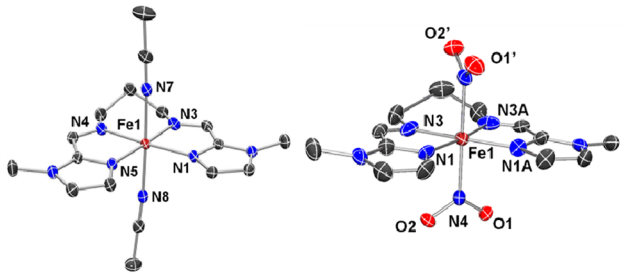


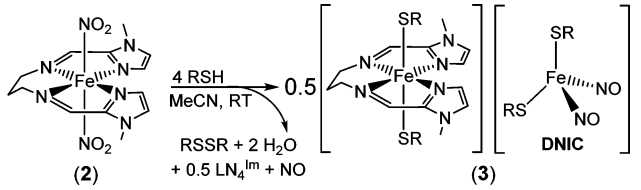
Figure 1. ORTEP of $\mathbf{1}^{MeCN}$ (left) and **2** (right) with 50% thermal probability for all non-hydrogen atoms. MeCN and PhCN solvent of crystallization for $\mathbf{1}^{MeCN}$ and **2**, respectively, have been omitted for clarity.

exception to the LS trend; however, the binding of the second axial NO_2^- group is a first in Fe^{II} heme and nonheme systems. The π-acidity of NO_2^- in **2** is likely buffered by the neutral, less basic LN_4^{Im}. In contrast, Fe–P complexes with other anionic axial ligands are typically high-spin.[13]

X-ray crystallographic analysis revealed distorted octahedral Fe^{II} centers from the four basal plane N-donors of LN_4^{Im} and two MeCN or NO_2^- axial ligands for $\mathbf{1}^{MeCN}$ and **2**, respectively (Figure 1). The bond distances for $\mathbf{1}^{MeCN}$ and **2** are similar to Fe–N_{imine} (avg: 1.962 Å for **1**; 1.940 Å for **2**) and Fe–$N_{imidazole}$ (avg: 1.992 Å for **1**; 1.996 Å for **2**) lengths supportive of the LS nature of Fe^{II}. The axial Fe–NCMe distance (avg: 1.935 Å) in $\mathbf{1}^{MeCN}$ is shorter than the Fe–NO_2 distance (avg: 1.964 Å) in **2** reflective of the better π-accepting ability of nitrile versus nitrite. Comparison of the Fe–NO_2 distance in **2** with Fe^{II}–P–NO_2 complexes emphasizes the highly variable nature of the π-bonding in the NO_2^- ligand. For example, the Fe–NO_2 distance of **2** is longer than the Fe–NO_2 distance in the five-coordinate Fe^{II}–P–NO_2 complex (1.849 Å)[13] and *cc* NiR (1.9 Å, Fe^{III} form),[14] but similar to that found in six-coordinate Fe^{II}–P–NO_2 complexes (avg: 1.988 Å).[15] This structural discrepancy in five- versus six-coordinate Fe–NO_2 complexes has been attributed to the trans influence, i.e. competition for the d_π orbitals of Fe.[16] For comparison, the only Fe-axial-dinitro complex that has been characterized by X-ray diffraction is an *Fe^{III}-P* species with Fe–NO_2(avg): 1.985 Å.[17] Complex **2** is thus the first structurally characterized *Fe^{II}*-axial-dinitro complex and shares metric similarities to six-coordinate mononitro Fe^{II}–P–NO_2 complexes. The unique N–O distances in **2** (one long: 1.285 Å; one short: 1.222 Å) are symptomatic of the diminished π-delocalization in the O–N–O molecule and underscores the potential lability of these bonds (vide infra).

The unprecedented $Fe(NO_2)_2$ axial ligation in **2** prompted us to explore its reaction chemistry with thiols since they could function as H^+ and e^- sources for reduction of coordinated NO_2^-. Reaction of **2** with *p*-chlorobenzenethiol (1:4; *p*-ClArSH = RSH, pK_a: 9–10 in DMSO[18]) resulted in the tetrahedral dinitrosyl iron complex (DNIC), $[Fe(SAr\text{-}p\text{-}Cl)_2(NO)_2]^-$ (anion of **3**, MeCN, room temperature = RT; see Scheme 2). Fractional precipitation of the reaction mixture allowed us to characterize the products formed. After reacting **2** with RSH (1:4) for 24 h, the solvent was removed and the dark residue was treated with Et_2O to afford an insoluble dark-red solid. Spectroscopic analysis of this solid by FTIR (ν_{NO}: 1743, 1692 cm^{-1}, KBr), UV–vis (λ_{max}: 487, 790 nm, MeCN), and ESI-MS(−) is consistent with DNIC (73%).[19] This assignment was further verified by comparing these parameters to that of

Scheme 2. Proposed Reaction of 2 with RSH (R: *p*-ClArSH)



independently prepared **3** (Et_4N^+ salt, Figures S5–S7). ESI-MS(+) of this solid confirmed that a possible cation of **3** is the Fe^{III} complex $[Fe(LN_4^{Im})(SR)_2]^+$ (Figures S8–S9). The organic soluble materials comprised the disulfide of *p*-Cl-ArSH (*p*-Cl-ArSSAr-*p*-Cl or RSSR) and free LN_4^{Im} (^{1}H NMR compared to authentic samples). Based on this evidence, one mechanistic proposal involves the stepwise heterolytic cleavage of the N–O bonds in **2** and formation of a transient mononitrosyl {FeNO}^{7} iron complex (MNIC). All RSH equivalents serve as H^+ sources; half reduces the {FeNO} unit (generating RSSR), and the other half becomes a ligand. Recent work from Kim demonstrated that Fe-thiolate MNICs disproportionate into DNIC and 2Fe–2S clusters in the presence of excess thiol.[20] A similar fate in the present reaction thus appears reasonable. Moreover, thiol (not thiolate) is necessary for the observed conversion as the addition of (Et_4N)(SAr-*p*-Cl) to an MeCN solution of **2** does not yield DNIC. Thus, a proton-coupled redox event accounts for the chemistry in Scheme 2.

The **2** and RSH reaction represents a new path to NO formation and interception via the DNIC. Indeed, studies in the early 1980s revealed the in vivo formation of protein-bound DNICs when rats were fed diets high in nitrite salts.[21,22] DNIC formation is in contrast to the reaction of Fe^{III}–P–NO_2 complexes with thiols, which yield the corresponding {FeNO}^{7} and sulfenic acid (RS═OH) through an O atom transfer (OAT) mechanism.[23] No evidence for S-oxygenates was observed in the **2** and RSH reaction demonstrating the difference in chemistry between Fe^{III}– and Fe^{II}–NO_2 complexes. Moreover, addition of 25 mol equiv of the classic O atom acceptor PPh_3[23b,24] resulted in no reaction with **2** under identical conditions (Figure S10). Although thiol-induced rearrangement of the coordination sphere of **2** to yield **3** halts catalytic NO_2^- reduction, the chemistry is indicative of the NiR activity of **2** in the presence of a weak acid, a previously uninvestigated H^+/e^- source for reduction of Fe^{II}–NO_2 complexes.

To circumvent DNIC formation, we tested the NiR activity of **2** using an acid with a non-coordinating conjugate base in combination with *p*-ClArSH as the sacrificial reductant. The reaction of **2** with a 1:1 mixture of tosic acid hydrate (TsOH·H_2O; pK_a: 8.6, MeCN[25])/*p*-ClArSH (1:2:2, net: 2H$^+$, 1 e$^-$ per bound NO_2^-) resulted in an immediate color change of the MeCN solution from violet to red. The first indication that this pathway was different from the thiol-only reaction was from fractional precipitation of the reaction mixture. For example, removal of the MeCN solvent followed by treatment of the dark residue with Et_2O afforded the red insoluble Fe-containing product, $[Fe^{II}(LN_4^{Im})(MeCN)_2](TsO)_2$ (tosylate salt of $\mathbf{1}^{MeCN}$) in 73% yield (UV–vis, FTIR, and ESI-MS(+)). The FTIR of the Et_2O-insoluble compound displayed no ν_{NO} peaks attributed to DNIC.[26] Furthermore, ^{1}H NMR analysis of the Et_2O-soluble portion indicated only RSSR (85%).

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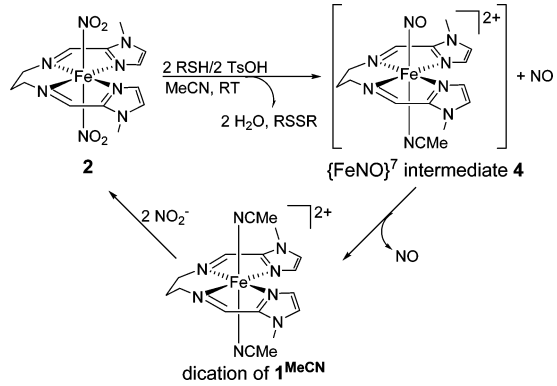
Further insight regarding the fate of the NO_2^- ligands of **2** was obtained through GC-MS analysis of the reaction headspace. Sampling the headspace after mixing **2** with RSH/TsOH (1:2:2) under the same conditions stated previously revealed the presence of a peak in the GC (t_r = 1.79 min) whose corresponding MS (m/z: 29.9) was consistent with NO (Figure S11). There was no evidence for other nitrogen oxide compounds (i.e., N_2O, NO_2). Control experiments with NO_2^- resulted in ∼10% of the NO observed in the **2**-promoted reduction highlighting its requirement in the NO_2^--to-NO conversion. An identical GC-MS experiment with ^{15}N-labeled $\mathbf{2}^{\mathbf{15N}}$ exhibited m/z: 30.9 (^{15}NO) to further corroborate NO formation from **2** (Figure S12). To quantify released NO(g), vial-to-vial NO-trapping reactions were performed with the Co^{II}–P complex [Co(T(−OMe)PP)] (where T(−OMe)PP = 5,10,15,20,-tetrakis(4-methoxyphenyl)-21*H*,23*H*-porphine) to generate the corresponding $\{CoNO\}^8$ complex [Co(T-(−OMe)PP)(NO)].[9d] Performing this experiment with **2** and RSH/TsOH (1:2:2) resulted in stoichiometric conversion of [Co(T(−OMe)PP)] to the $\{CoNO\}^8$ complex as monitored by UV–vis (λ_{max}: 418, 540 nm, CH_2Cl_2) and FTIR (ν_{NO}: 1697 cm^{-1}; ν_{15NO}: 1667 cm^{-1} using $\mathbf{2}^{\mathbf{15N}}$, KBr, Figures S13–S14).

The release of NO from the reaction of **2** and RSH/TsOH, coupled with the isolation of $\mathbf{1}^{\mathbf{MeCN}}$, suggested we could reform **2** by addition of NO_2^- to the reaction mixture and demonstrate turnover. Thus, the formation of NO was monitored by GC-MS under identical conditions (vide supra). After 15 min, 2 mol equiv of NO_2^- were added to the mixture to displace any coordinated NO and regenerate **2**. GC-MS analysis of the reaction headspace at this point verified the presence of NO (Figure S15). After this measurement, the headspace was removed under vacuum and refilled with N_2 to provide an NO-free baseline in the GC. Subsequent iterations of this cycle (three total) demonstrated the turnover of NO_2^- to NO via **2** and RSH/H^+, generation of $\mathbf{1}^{\mathbf{MeCN}}$, and last reformation of **2** with added NO_2^-. Notably, the Fe-catalyst **2** is recoverable after three cycles in 80% yield (cycles 2 and 3 reveal 97 and 84% headspace NO with respect to cycle 1).[26] Overall, these results provide strong support that **2** is a functional NiR model.

NO formation from Fe–NO_2 complexes occurs through three mechanisms: (i) OAT to an acceptor molecule (E) to produce the $\{FeNO\}^7$ product and E=O;[23a,b,24] (ii) H^+-assisted reduction and heterolysis of the N–O bond through loss of O^{2-} (as H_2O; μ-oxo bridge when Lewis acid (Cu^I) used in place of H^+) and formation of an $\{FeNO\}^7$ complex (via transient $\{FeNO\}^6$);[10a−d] and (iii) H^+-assisted reduction and homolysis of the N–O bond to afford Fe^{III}–OH and NO.[10e] Not surprisingly, we can rule out (i), as excess PPh_3 does not react with **2** (vide supra). Pathway (iii) can also be eliminated since this route generally requires an *O*-bound (nitrito) NO_2^- ligand. X-ray crystallographic analysis of **2** under several different growth conditions always resulted in N-bound nitrite ligands. The IR spectrum of **2** is also suggestive of nitro coordination.[12] Taken together, (ii) is the most reasonable path.

A probable mechanism emerges and is supported by several lines of evidence (Scheme 3). Bulk workup and analysis of the reaction of **2** and RSH/TsOH reveals formation of $\mathbf{1}^{\mathbf{MeCN}}$ (Et_2O-insoluble) and RSSR (Et_2O-soluble) in ∼80% yield. Furthermore, trapping of NO from this reaction with Co^{II}–P establishes the stoichiometric release of NO. In the absence of an NO acceptor, mechanism (ii) would suggest an $\{FeNO\}^7$ (**4** in Scheme 3) or $\{Fe(NO)_2\}^8$ intermediate is likely traversed.

Scheme 3. Reaction Path of 2 with RSH/TsOH



Our results support the former. First, the $\{Fe(NO)_2\}^8$ formulation has only been proposed as a *transient* (low temperature) intermediate in three instances.[27] Second, attempts at synthesizing this FeNO species by reacting NO with **1** only result in a product with one strong ν_{NO} stretch in the IR (∼1700 cm^{-1}),[28] which is consistent with $\{FeNO\}^7$ complexes in similar coordination environments.[29] Finally, in situ monitoring of the **2** and RSH/TsOH reaction revealed IR and UV–vis features that resemble independently prepared **4** (Figure S16). We hypothesized that the Fe–NO bond in **4** would be particularly labile. This logic stems from the decreased basicity of LN_4^{Im} (compared to a previously reported $\{FeNO\}^7$ complex with pyrrole ligands)[11] making the Fe center less of a π-donor. Also, LN_4^{Im} bears some resemblance, in an electronic sense, to the neutral N_4Py ligand (N4Py = *N*,*N*-bis(2-pyridylmethyl)-(*N*-(bis-2-pyridylmethyl)amine)) whose corresponding $\{FeNO\}^7$ complex exhibits a *labile* Fe–NO bond.[30] The Fe–NO bond lability in **4** is further confirmed in its synthesis, as application of vacuum or simple dissolution in donor solvents ultimately yields $\mathbf{1}^{\mathbf{S}}$ making isolation of analytically pure **4** difficult.

In summary, we report the synthesis and properties of two nonheme Fe^{II} complexes with special emphasis on the dinitro complex **2**, which displays stoichiometric and catalytic NiR activity. To our knowledge, **2** represents the first nonheme complex that demonstrates selective turnover of NO_2^- into NO. Additionally, **2** is the first structurally characterized example of a nonheme complex with *trans* coordinated nitro ligands.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Details of the syntheses and crystallographic (CIF) results. 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, L. J. *Nitric Oxide Biology and Pathobiology*; Academic Press: San Diego, 2000. (b) Moncada, S.; Higgs, E. A. *Br. J. Pharmacol.* **2006**, *147*, S193. (c) Hill, B. G.; Dranka, B. P.; Bailey, S. M.; Lancaster, J. R., Jr.; Darley-Usmar, V. M. *J. Biol. Chem.* **2010**, *285*, 19699.

(2) (a) van Faassen, E. E.; Bahrami, S.; Feelisch, M.; Hogg, N.; Kelm, M.; Kim-Shapiro, D. B.; Kozlov, A. V.; Li, H.; Lundberg, J. O.; Mason, R.; et al. *Med. Res. Rev.* **2009**, *29*, 683. (b) Lundberg, J. O.; Weitzberg, E.; Gladwin, M. T. *Nat. Rev. Drug Discovery* **2008**, *7*, 156. (c) Maia, L. B.; Moura, J. J. G. *Chem. Rev.* **2014**, *114*, 5273. (d) Gladwin, M. T.; Grubina, R.; Doyle, M. P. *Acc. Chem. Res.* **2009**, *42*, 157. (e) Ormerod, J. O. M.; Ashrafian, H.; Maher, A. R.; Arif, S.; Steeples, V.; Born, G. V. R.; Egginton, S.; Feelisch, M.; Watkins, H.; Frenneaux, M. P. *Cardiovasc. Res.* **2011**, *89*, 560.

(3) (a) Fukuto, J. M.; Cisneros, C. J.; Kinkade, R. L. *J. Inorg. Biochem.* **2013**, *118*, 201. (b) Sanders, B. C.; Rhine, M. A.; Harrop, T. C. *Struct. Bonding (Berlin)* **2014**, *160*, 57.

(4) (a) Wang, R. *Physiol. Rev.* **2012**, *92*, 791. (b) Kabil, O.; Banerjee, R. *J. Biol. Chem.* **2010**, *285*, 21903.

(5) WHO *Background document for development of WHO Guidelines for Drinking-water Quality* 2011, *WHO/SDE/WSH/07.01/16/Rev/1*.

(6) Grant, S. B.; Saphores, J.-D.; Feldman, D. L.; Hamilton, A. J.; Fletcher, T. D.; Cook, P. L. M.; Stewardson, M.; Sanders, B. F.; Levin, L. A.; Ambrose, R. F.; Deletic, A.; Brown, R.; Jiang, S. C.; Rosso, D.; Cooper, W. J.; Marusic, I. *Science* **2012**, *337*, 681.

(7) (a) Dezfulian, C.; Raat, N.; Shiva, S.; Gladwin, M. T. *Cardiovasc. Res.* **2007**, *75*, 327. (b) Pattillo, C. B.; Bir, S.; Rajaram, V.; Kevil, C. G. *Cardiovasc. Res.* **2011**, *89*, 533. (c) Duranski, M. R.; Greer, J. J. M.; Dejam, A.; Jaganmohan, S.; Hogg, N.; Langston, W.; Patel, R. P.; Yet, S.-F.; Wang, X.; Kevil, C. G.; Gladwin, M. T.; Lefer, D. J. *J. Clin. Invest.* **2005**, *115*, 1232.

(8) (a) Tolman, W. B. *J. Biol. Inorg. Chem.* **2006**, *11*, 261. (b) Wasser, I. M.; de Vries, S.; Moënne-Loccoz, P.; Schröder, I.; Karlin, K. D. *Chem. Rev.* **2002**, *102*, 1201. (c) Woollard-Shore, J. G.; Holland, J. P.; Jones, M. W.; Dilworth, J. R. *Dalton Trans.* **2010**, *39*, 1576.

(9) (a) Chen, C. S.; Yeh, W. Y. *Chem. Commun.* **2010**, *46*, 3098. (b) Chuang, W.-J.; Lin, I.-J.; Chen, H.-Y.; Chang, Y.-L.; Hsu, S. C. N. *Inorg. Chem.* **2010**, *49*, 5377. (c) Kujime, M.; Izumi, C.; Tomura, M.; Hada, M.; Fujii, H. *J. Am. Chem. Soc.* **2008**, *130*, 6088. (d) Kumar, M.; Dixon, N. A.; Merkle, A. C.; Zeller, M.; Lehnert, N.; Papish, E. T. *Inorg. Chem.* **2012**, *51*, 7004. (e) Maji, R. C.; Barman, S. K.; Roy, S.; Chatterjee, S. K.; Bowles, F. L.; Olmstead, M. M.; Patra, A. K. *Inorg. Chem.* **2013**, *52*, 11084. (f) Halfen, J. A.; Tolman, W. B. *J. Am. Chem. Soc.* **1994**, *116*, 5475. (g) Halfen, J. A.; Mahapatra, S.; Wilkinson, E. C.; Gengenbach, A. J.; Young, V. G. J.; Que, L. J.; Tolman, W. B. *J. Am. Chem. Soc.* **1996**, *118*, 763.

(10) (a) Ching, W.-M.; Chuang, C.-H.; Wu, C.-W.; Peng, C.-H.; Hung, C.-H. *J. Am. Chem. Soc.* **2009**, *131*, 7952. (b) Harris, T. D.; Betley, T. A. *J. Am. Chem. Soc.* **2011**, *133*, 13852. (c) López, J. P.; Heinemann, F. W.; Prakash, R.; Hess, B. A.; Horner, O.; Jeandey, C.; Oddou, J.-L.; Latour, J.-M.; Grohmann, A. *Chem.—Eur. J.* **2002**, *8*, 5709. (d) Villar-Acevedo, G.; Nam, E.; Fitch, S.; Benedict, J.; Freudenthal, J.; Kaminsky, W.; Kovacs, J. A. *J. Am. Chem. Soc.* **2011**, *133*, 1419. (e) Tsou, C.-C.; Yang, W.-L.; Liaw, W.-F. *J. Am. Chem. Soc.* **2013**, *135*, 18758.

(11) (a) Patra, A. K.; Dube, K. S.; Sanders, B. C.; Papaefthymiou, G. C.; Conradie, J.; Ghosh, A.; Harrop, T. C. *Chem. Sci.* **2012**, *3*, 364. (b) Sanders, B. C.; Patra, A. K.; Harrop, T. C. *J. Inorg. Biochem.* **2013**, *118*, 115.

(12) Nakamoto, K. *Infrared and Raman Spectra of Inorganic and Coordination Compounds*; John Wiley & Sons, Ltd., 1978.

(13) Nasri, H.; Wang, Y.; Huynh, B. H.; Scheidt, W. R. *J. Am. Chem. Soc.* **1991**, *113*, 717.

(14) Einsle, O.; Messerschmidt, A.; Huber, R.; Kroneck, P. M. H.; Neese, F. *J. Am. Chem. Soc.* **2002**, *124*, 11737.

(15) Nasri, H.; Ellison, M. K.; Krebs, C.; Huynh, B. H.; Scheidt, W. R. *J. Am. Chem. Soc.* **2000**, *122*, 10795.

(16) Optimal π-overlap between Fe and NO_2^- results when the two O−N−O planes are orthogonal to each other to interact separately with the d_{xz} and d_{yz} orbitals. The rotational disorder of the NO_2^- ligands in **2** makes it impossible to comment on such an orientation.

(17) Nasri, H.; Goodwin, J. A.; Scheidt, W. R. *Inorg. Chem.* **1990**, *29*, 185.

(18) Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1982**, *47*, 3224.

(19) (a) Hung, M.-C.; Tsai, M.-C.; Lee, G.-H.; Liaw, W.-F. *Inorg. Chem.* **2006**, *45*, 6041. (b) Harrop, T. C.; Tonzetich, Z. J.; Reisner, E.; Lippard, S. J. *J. Am. Chem. Soc.* **2008**, *130*, 15602. (c) Tsai, F.-T.; Kuo, T.-S.; Liaw, W.-F. *J. Am. Chem. Soc.* **2009**, *131*, 3426.

(20) Fitzpatrick, J.; Kalyvas, H.; Filipovic, M. R.; Ivanović-Burmazović, I.; MacDonald, J. C.; Shearer, J.; Kim, E. *J. Am. Chem. Soc.* **2014**, *136*, 7229.

(21) Woolum, J. C.; Commoner, B. *Biochim. Biophys. Acta* **1970**, *201*, 131.

(22) The H^+-assisted reaction of free NO_2^- with RSH yields the corresponding *S*-nitrosothiol (RSNO), which is a potential source of NO; see: Koppenol, W. H. *Inorg. Chem.* **2011**, *51*, 5637. Mixing **1** with Ph_3CSNO (1:2) in MeCN for 18 h resulted in no DNIC.

(23) (a) Heinecke, J.; Ford, P. C. *J. Am. Chem. Soc.* **2010**, *132*, 9240. (b) Heinecke, J. L.; Khin, C.; Pereira, J. C. M.; Suárez, S. A.; Iretskii, A. V.; Doctorovich, F.; Ford, P. C. *J. Am. Chem. Soc.* **2013**, *135*, 4007. (c) Nasri, H.; Haller, K. J.; Wang, Y.; Huynh, B. H.; Scheidt, W. R. *Inorg. Chem.* **1992**, *31*, 3459.

(24) Patra, A. K.; Afshar, R. K.; Rowland, J. M.; Olmstead, M. M.; Mascharak, P. K. *Angew. Chem., Int. Ed.* **2003**, *42*, 4517.

(25) Kütt, A.; Leito, I.; Kaljurand, I.; Sooväli, L.; Vlasov, V. M.; Yagupolskii, L. M.; Koppel, I. A. *J. Org. Chem.* **2006**, *71*, 2829.

(26) Trace amounts of the dinuclear species, $[Fe_2(\mu\text{-}SR)_2(NO)_4]$ = Roussin's red ester, are observed in the IR and likely accounts for the less than stoichiometric recovery of **2**.

(27) (a) Patterson, J. C.; Lorković, I. M.; Ford, P. C. *Inorg. Chem.* **2003**, *42*, 4902. (b) Wang, J.; Schopfer, M. P.; Sarjeant, A. A. N.; Karlin, K. D. *J. Am. Chem. Soc.* **2009**, *131*, 450. (c) Lorković, I.; Ford, P. C. *J. Am. Chem. Soc.* **2000**, *122*, 6516.

(28) Weak ν_{NO} signals at ∼1800 cm^{-1} are observed in attempted preparations of **4**. While this may be assigned to an $\{Fe(NO_2)\}^8$ complex, the low intensity with respect to the strong peak at ∼1700 cm^{-1} leads us to think otherwise. It is possible that a mixture of five- and six-coordinate $\{FeNO\}^7$ is present, which have very different ν_{NO} values (see ref 29b).

(29) (a) McCleverty, J. A. *Chem. Rev.* **2004**, *104*, 403. (b) Goodrich, L. E.; Paulat, F.; Praneeth, V. K. K.; Lehnert, N. *Inorg. Chem.* **2010**, *49*, 6293.

(30) McQuilken, A. C.; Ha, Y.; Sutherlin, K. D.; Siegler, M. A.; Hodgson, K. O.; Hedman, B.; Solomon, E. I.; Jameson, G. N. L.; Goldberg, D. P. *J. Am. Chem. Soc.* **2013**, *135*, 14024.