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# Dinitrosyl Iron Complexes (DNICs) Bearing O-Bound Nitrito Ligand: Reversible Transformation between the Six-Coordinate $\{Fe(NO)_2\}^9$ $[(1\text{-MeIm})_2(\eta^2\text{-ONO})Fe(NO)_2]$ ($g = 2.013$) and Four-Coordinate $\{Fe(NO)_2\}^9$ $[(1\text{-MeIm})(ONO)Fe(NO)_2]$ ($g = 2.03$)

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Dinitrosyl iron complexes (DNICs), one of the possible forms for storage and transport of NO, have been known to exert NO bioactivity under physiological and pathological conditions.[1,2] It is proposed that DNICs play a crucial role in regulating iron uptake/storage, triggering the expression of proteins against nitrosative stress, and reassembling [Fe−S] clusters after nitrosative damage.[3] Characterization of DNICs in vitro/vivo has been made possible via the distinct EPR signal at $g = 2.03$.[1−3] Nitrite, an ubiquitous molecule in vivo, particularly in the endocrine system, serves in intravascular NO storage/transport in blood circulation.[4] Nitrite signaling operates through the cooperative action with hemes, thiols, amines, polyphenols, and ascorbate yielding nitric oxide during physiological and pathological hypoxia.[5a] In particular, the biotransformation of nitroglycerin (GTN) in the presence of cysteine/NADH generating NO and nitrite was proposed to proceed via the nitrite-containing ferrous intermediate (Supporting Information (SI) Scheme S1).[5b]

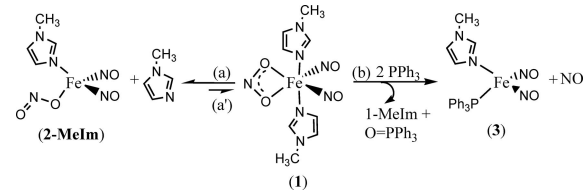
DNICs containing the various ligation modes [S,S]/[S,O]/[S,N]/[N,N] were recently synthesized.[6] In spite of the few O-bound monodentate nitrito/chelating nitrito complexes such as *cis*-$[Fe(NO)(NO_2)(TC\text{-}5,5)]$ and $[HB(3,5\text{-}Me_2pz)_3Fe(\eta^2\text{-ONO})Cl]^-$ reported,[7] no discrete nitrite-containing DNICs are known. In this contribution, the temperature-dependent reversible transformation between the six-coordinate chelating nitrito $\{Fe(NO)_2\}^9$ DNIC $[(1\text{-MeIm})_2(\eta^2\text{-ONO})Fe(NO)_2]$ (1-MeIm = 1-methylimidazole) (**1**) and the four-coordinate monodentate nitrito $\{Fe(NO)_2\}^9$ DNIC $[(1\text{-MeIm})(ONO)Fe(NO)_2]$ (**2-MeIm**) was demonstrated.[8] Transformation of an O-bound nitrito ligand of complex **1** into NO promoted by $PPh_3$ accompanied by the formation of $\{Fe(NO)_2\}^{10}$ $[(1\text{-MeIm})(PPh_3)Fe(NO)_2]$ (**3**) was also elucidated.

Reaction of $[Fe(CO)_2(NO)_2]^+$ with 1 equiv of $[NO_2]^-$ and 2 equiv of 1-MeIm in THF at −10 °C led to the isolation of the chelating nitrito $\{Fe(NO)_2\}^9$ $[(1\text{-MeIm})_2(\eta^2\text{-ONO})Fe(NO)_2]$ (**1**) characterized by IR (1749 vs 1820 s $cm^{-1}$ (MeOH)) and EPR spectroscopies and single-crystal X-ray crystallography. In the isotopic labeling experiments, the IR spectrum of complex **1** exhibits a diagnostic $\nu_{O-N-O}$ vibrational frequency of the bidentate nitrito ligand ($^{15}NO_2^-$) at 1248 $cm^{-1}$, shifting from 1261 $cm^{-1}$ (KBr).

The variable temperature EPR spectra demonstrate that the thermal transformation occurred between the neutral six-coordinate DNIC **1** and the neutral four-coordinate **2-MeIm** in THF (Scheme 1a and 1a′). To corroborate the existence of **2-MeIm**, the analogue $[(HIm)(ONO)Fe(NO)_2]$ (HIm = imidazole) (**2-HIm**) was synthesized with IR $\nu_{NO}$ stretching frequency 1729 vs 1800 s $cm^{-1}$ (MeOH) and $\nu_{N-O}$ of the O-bound nitrito 1269 $cm^{-1}$ (KBr, $\nu^{15}{}_{N-O}$ 1249 $cm^{-1}$). The variable temperature EPR spectrum of complex **2-HIm** displays a well-resolved nine-line hyperfine splitting with $g = 2.031$ ($a_{NO} = 2.60$ G and $a_{HIm} = 4.81$ G) at 180 K (SIFigure S1). As shown in Figure 1a−b and also in SIFigure S2, EPR studies were performed at 300, 220, 180, and 160 K for identification and detection of species formed via transformation of complex **1**. Complex **1** dissolved in THF exhibits a well-resolved nine-line hyperfine splitting with a $g$ value of 2.031 at 220 K. This EPR spectrum, identical to the EPR spectrum of complex **2-HIm** characterized by single-crystal X-ray crystallography, indicates the formation of the four-coordinate complex **2-MeIm**.[9] At 180 K, the EPR spectrum exhibits a well-resolved nine-line hyperfine splitting with a $g$ value of 2.030 ($a_{NO} = 2.60$ G and $a_{1\text{-MeIm}} = 4.81$ G) along with the appearance of a well-resolved thirteen-line hyperfine splitting with a $g$ value of 2.013 ($a_{NO} = 5.78$ G and $a_{1\text{-MeIm}} = 9.21$ G) assigned to the spectrum of complex **1** (Figure 1b). (Under the presence of 100-fold 1-MeIm, the EPR spectrum of complex **1** displays a well-resolved thirteen-line hyperfine splitting with a $g$ value of 2.013 in $CH_2Cl_2$ at 180 K ($a_{NO} = 5.11$ G and $a_{1\text{-MeIm}} = 8.63$ G) (SIFigure S3).) This result demonstrates that complexes **1** and **2-MeIm** undergo a temperature-dependent reversible transformation (dynamic equilibrium).

Figure 2a and 2b display the thermal ellipsoid plots of the neutral complexes **1** and **2-HIm**, respectively, and the selected bond lengths and bond angles are given in the figure captions, respectively. It is

***Scheme 1***



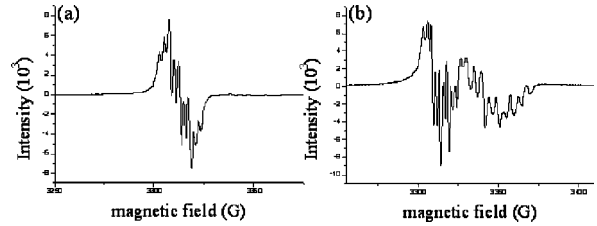




***Figure 1.*** EPR spectra of the thermal transformation between complex **1** and **2-MeIm** in THF solution at (a) 220 K (complex **2-MeIm** ($g_{av} = 2.031$, $a_{NO} = 2.60$ G, $a_{1\text{-MeIm}} = 4.81$ G)), (b) 180 K (complex **1** ($g_{av} = 2.013$, $a_{NO} = 5.78$ G, $a_{1\text{-MeIm}} = 9.21$ G) and complex **2-MeIm** ($g_{av} = 2.031$, $a_{NO} = 2.60$ G, $a_{1\text{-MeIm}} = 4.81$ G)).

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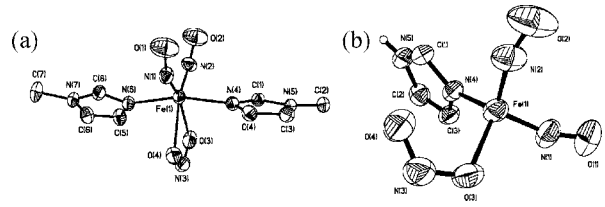


***Figure 2.*** ORTEP drawing and labeling scheme of complexes **1** and **2-HIm** with thermal ellipsoids drawn at 50% probability. Selected bond lengths (Å) and angles (deg): (a) Fe(1)−N(1) 1.724(3), Fe(1)−N(2) 1.718(3), Fe(1)−N(4) 2.113(2), Fe(1)−N(6) 2.143(2), Fe(1)−O(3) 2.306(2), Fe(1)−O(4) 2.286(3), N(1)−O(1) 1.172(4), N(2)−O(2) 1.155(4), N(3)−O(3) 1.259(4), N(3)−O(4) 1.263(4); Fe(1)−N(1)−O(1) 149.3(3), Fe(1)−N(2)−O(2) 151.0(3), O(3)−Fe(1)−O(4) 54.31(10), O(3)−N(3)−O(4) 112.4(3). (b) Fe(1)−N(1) 1.692(3), Fe(1)−N(2) 1.681(3), Fe(1)−N(4) 2.007(2), Fe(1)−O(3) 1.992(2), N(1)−O(1) 1.173(4), N(2)−O(2) 1.171(4), N(3)−O(3) 1.284(4), N(3)−O(4) 1.206(4);Fe(1)−N(1)−O(1)162.7(3),Fe(1)−N(2)−O(2)163.6(3),O(3)−N(3)−O(4) 113.3(3).

noticed that the Fe(1)−N(1) and Fe(1)−N(2) bond lengths of 1.724(3) and 1.718(3) Å in complex **1**, respectively, are longer than the reported Fe−N(O) bond lengths ranging from 1.661(4) to 1.695(3) Å of $\{Fe(NO)_2\}^9$ DNICs.[6,9] In contrast, the mean Fe−N(O) bond length of 1.685(3) Å (1.681(3) and 1.692(3) Å) in complex **2-HIm** falls in the range of the $\{Fe(NO)_2\}^9$ DNICs.[6,9] Also, the Fe(1)−N(1)−O(1) and Fe(1)−N(2)−O(2) bond angles of 149.3(3)° and 151.0(3)° in complex **1** are smaller than those of the published four-coordinate DNICs ranging from 157.1(2)° to 172.1(3)°.[6,9] The (Fe)O(3)−N(3) bond length of 1.284(4) Å in the O-bound nitrito complex **2-HIm**, compared to those of 1.259(4) and 1.263(4) Å in complex **1**, is significantly longer than the distal N(3)−O(4) bond length of 1.206(4) Å.[7b]

To investigate the activation of nitrite yielding nitric oxide, reaction of complex **1** with 2 equiv of $PPh_3$ was conducted. In contrast to the inertness of complex **2-HIm** toward $PPh_3$, addition of 2 equiv of $PPh_3$ into complex **1** promotes O-atom transfer of the chelating nitrito under mild conditions to generate $OPPh_3$ ($^{31}P$ NMR: $\delta$ = 29.2 ppm in $CDCl_3$),[10] the neutral EPR-silent $\{Fe(NO)_2\}^{10}$ [(1-MeIm)($PPh_3$)Fe($NO)_2$] (**3**) identified by IR and UV−vis spectroscopies and single-crystal X-ray crystallography (SIFigure S4), and the released NO trapped by $[PPN]_2[S_5Fe(\mu\text{-}S)_2FeS_5]$ generating the corresponding $[PPN][S_5Fe(NO)_2]$ in THF−MeCN.[9] The mechanism of transformation of complex **1** into complex **3** can be rationalized as the following reaction sequences (SIScheme S2); intermediate [(1-MeIm)$_2$(NO)Fe($NO)_2$] (**A**) containing the nitroxyl anion ($NO^-$) coordinated ligand (nitrite-to-nitroxyl conversion) was proposed to be produced upon O-atom transfer to $PPh_3$, the sequential reductive elimination of NO, and the concomitant ligand substitution of 1-MeIm by $PPh_3$ yields complex **3**.

In summary, in contrast to tetrahedral $\{Fe(NO)_2\}^9$ DNICs with an EPR $g$ value of 2.03, the nonclassical six-coordinate $\{Fe(NO)_2\}^9$ DNIC **1** displays an EPR signal $g$ = 2.013. The temperature-dependent reversible transformation occurs between DNIC **1** and DNIC **2-MeIm**. The chelating nitrito of $\{Fe(NO)_2\}^9$ DNIC **1**, triggered by $PPh_3$, undergoes O-atom transfer to result in reductive elimination of NO along with the generation of $\{Fe(NO)_2\}^{10}$ DNIC **3**, in contrast to the inertness of the nitrite-containing $\{Fe(NO)_2\}^9$ DNIC **2-HIm** toward $PPh_3$. The findings, EPR signals of $g$ = 2.013 for complex **1** and $g$ = 2.03 for complexes **2-MeIm/2-HIm**, imply that characterization of DNICs in vitro/in vivo may be possible via their distinctive EPR signal $g$ = 2.03 for the tetrahedral DNICs and EPR signal $g$ = 2.01 for the six-coordinate DNICs. This result may signify that nitrite-containing $\{Fe(NO)_2\}^9$ DNICs may serve as the transient intermediates for the conservation of NO bioactivity under biological conditions, and the nonclassical six-coordinate nitrite-containing $\{Fe(NO)_2\}^9$ DNICs may act as an active center to trigger the transformation of nitrite into nitric oxide in biological systems.[11] Studies of the electronic structure and reactivity of complexes **1** and **2-HIm** are underway.

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**Supporting Information Available:** X-ray crystallographic files in CIF format for the structure determinations of [(1-MeIm)$_2$($\eta^2$-ON-O)Fe($NO)_2$], [(HIm)(ONO)Fe($NO)_2$], and [(1-MeIm)($PPh_3$)Fe($NO)_2$]. This material is available free of charge via the Internet at http://pubs.acs.org.

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