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Neutral $\{Fe(NO)_2\}^9$ Dinitrosyliron Complex (DNIC) $[(SC_6H_4\text{-}o\text{-}NHCOPh)(Im)Fe(NO)_2]$ (Im = Imidazole): Interconversion among the Anionic/Neutral $\{Fe(NO)_2\}^9$ DNICs and Roussin's Red Ester

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A neutral $\{Fe(NO)_2\}^9$ dinitrosyliron complex (DNIC) $[(SC_6H_4\text{-}o\text{-}NHCOPh)(Im)Fe(NO)_2]$ (Im = imidazole; **2**) was prepared by the reaction of $[Fe(\mu\text{-}SC_6H_4\text{-}o\text{-}NHCOPh)(NO)_2]_2$ (**1**) and 2 equiv of imidazole. In the synthesis of the anionic $\{Fe(NO)_2\}^9$ DNIC $[(SC_6H_4\text{-}o\text{-}NHCOPh)_2Fe(NO)_2]^-$ (**3**), thiolate $[SC_6H_4\text{-}o\text{-}NHCOPh]^-$ triggers ligand substitution of DNIC **2** to yield DNIC **3**. At 298 K, complexes **2** and **3** exhibit well-resolved nine- and five-line electron paramagnetic resonance (EPR) signals at $g = 2.031$ and 2.029, respectively, the characteristic g value of DNICs. The facile interconversions among the neutral $\{Fe(NO)_2\}^9$ complex **2**, the anionic $\{Fe(NO)_2\}^9$ complex **3**, and Roussin's red ester **1** were demonstrated. The EPR spectrum (the pattern of hyperfine splitting) in combination with the IR ν_{NO} (the relative position of the ν_{NO} stretching frequencies) spectrum may serve as an efficient tool for the discrimination of the anionic $\{Fe(NO)_2\}^9$ DNICs, the neutral $\{Fe(NO)_2\}^9$ DNICs, and Roussin's red ester.

Dinitrosyliron complexes (DNICs) and *S*-nitrosothiols (RSNO) have been known to be two possible forms for storage and transport of NO in biological systems.[1] The binding of NO to Fe−S cluster-containing proteins or enzymes in mitochondria and thiol-rich proteins in the presence of free Fe yielded DNICs, and dinuclear $[Fe(\mu\text{-}SR)(NO)_2]_2$ (Roussin's red ester) has been intensely studied.[1−3] Three types of electron paramagnetic resonance (EPR)-active DNICs containing a wide range of S/N/O ligation have been proposed in biology.[4] In particular, the protein-bound DNICs, obtained through nitrosylation of human glutathione transferase P1-1 with a dinitrosyldiglutathionyliron complex in vitro/in vivo and characterized by X-ray crystallography, were reported recently.[3a] As has been known, characterization of both protein-bound and low-molecular-weight DNICs (LMW-DNICs) in vitro has been made possible via their characteristic EPR signals at $g = 2.03$.[1−4] On the basis of oxidation levels of the $\{Fe(NO)_2\}$ core of DNICs, the known stable LMW-DNICs in inorganic chemistry can be classified into the anionic, paramagnetic $\{Fe(NO)_2\}^9$ DNICs coordinated by thiolate ligands and the neutral, diamagnetic $\{Fe(NO)_2\}^{10}$ DNICs coordinated by CO-, PPh_3-, and N-containing ligands.[5−6] Recently, we have shown that the reversible interconversion between complex $[S_5Fe(NO)_2]^-$ and the $[S_5Fe(\mu\text{-}S)_2FeS_5]^{2-}$ cluster is consistent with reports of in vitro repair of nitric oxide modified [2Fe-2S] ferredoxin by cysteine desulfurase and L-cysteine.[7−8] We also demonstrated that the NO-releasing ability of the anionic $\{Fe(NO)_2\}^9$ $[(RS)_2Fe(NO)_2]^-$ is finely tuned by the coordinated thiolate ligands.[9] The objective of this study was to delineate the synthesis of the neutral $\{Fe(NO)_2\}^9$ DNICs $[(SC_6H_4\text{-}o\text{-}$

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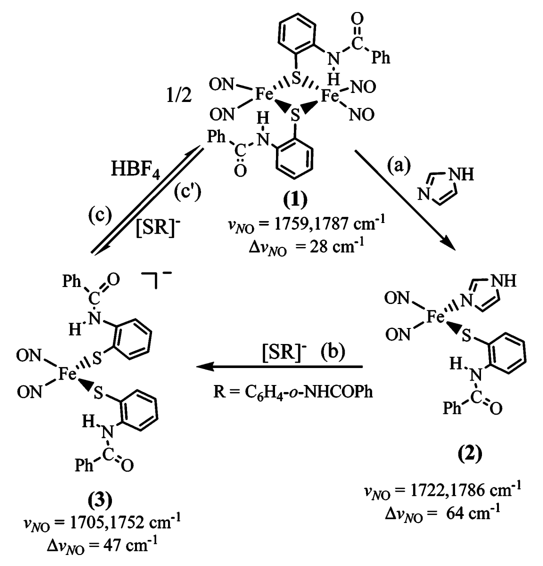
Scheme 1



NHCOPh)(Im)Fe(NO)$_2$] (Im = imidazole; **2**) and to investigate the interconversion among neutral $\{Fe(NO)_2\}^9$ DNICs **2**, anionic $\{Fe(NO)_2\}^9$ DNICs $[(SC_6H_4\text{-}o\text{-}NHCOPh)_2Fe(NO)_2]^-$ (**3**), and Roussin's red ester $[Fe(\mu\text{-}SC_6H_4\text{-}o\text{-}NHCOPh)(NO)_2]_2$ (**1**). The detailed spectroscopic analysis (EPR and IR ν_{NO} spectra) may provide a superior level of insight into the discrimination of the anionic $\{Fe(NO)_2\}^9$ DNICs, neutral $\{Fe(NO)_2\}^9$ DNICs, and Roussin's red ester.

The reaction of $Fe(CO)_2(NO)_2$ (0.2 mmol)[10] with $[SC_6H_4\text{-}o\text{-}NHCOPh]_2$ (0.092 g, 0.2 mmol) in tetrahydrofuran (THF) at ambient temperature yielded the dinuclear **1** as a brown-green solid isolated in 90% yield.[11] Complex **1** exhibits diagnostic IR ν_{NO} stretching frequencies at 1759 vs, 1787 vs, and 1815 vw cm^{-1} with $\Delta\nu_{NO}$ = 28 cm^{-1} ($\Delta\nu_{NO}$ is the separation of NO stretching frequencies 1759 and 1787 cm^{-1}). Consistent with other Roussin's red esters,[5a,11a] the dinuclear complex **1** was best described as a $\{Fe(NO)_2\}^9$–$\{Fe(NO)_2\}^9$ coupling, which is responsible for the absence of paramagnetism and the EPR signal.[11b]

Upon the addition of 2 equiv of imidazole (0.014 g, 0.2 mmol) to the THF solution of complex **1** (0.069 g, 0.1 mmol), a pronounced color change from brown-green to red-brown occurs at ambient temperature. The IR, UV–vis, EPR, and X-ray diffraction studies confirmed the formation of the neutral $\{Fe(NO)_2\}^9$ **2** (yield 0.077 g, 93%; Scheme 1a and Supporting Information S1).[12] The IR spectrum of complex **2** in THF reveals two ν_{NO} absorption bands at 1722 vs and 1786 vs cm^{-1} with $\Delta\nu_{NO}$ = 64 cm^{-1}. At 298 K, complex **2** exhibits a well-resolved nine-line EPR signal at g = 2.031 with hyperfine coupling constants of 2.4 and 4.1 G (Figure 1a).[5c] The conversion of complex **1** to **2** was also monitored by UV–vis spectrometry; the intense band at 438 nm disappeared, accompanied by the simultaneous formation of one absorption band at 450 nm (Supporting Information S2 and S3). As shown in Figure 2, analysis of the bond angles of complex **2** reveals that Fe is best described as existing in a tetrahedral coordination environment (Supporting Information S4 and S5). Also, the X-ray crystal structure of DNIC **2** shows that the N(5)–H(5A) bond tends to adopt intramolecular [N–H····S] interactions with a S(1)····N(5) distance of 2.986 Å.

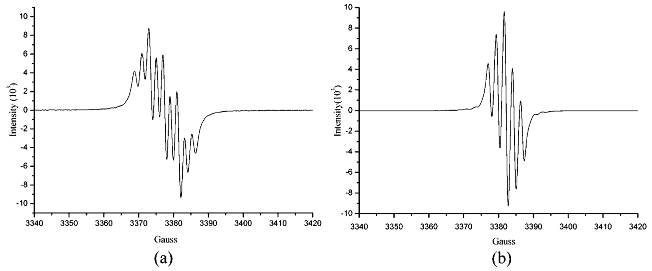


Figure 1. (a) EPR spectrum of DNIC **2** with g_{av} = 2.031 (a_{N1} = 2.4 G; a_{N3} = 4.1 G) at 298 K and (b) EPR spectrum of DNIC **3** with g_{av} = 2.0288 (a = 2.344 G) at 298 K.

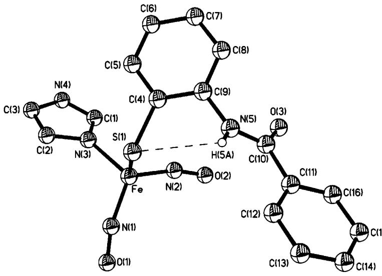


Figure 2. ORTEP drawing and labeling scheme of **2**with thermal ellipsoids drawn at 30% probability. Selected bond distances (Å) and angles (deg): Fe–N(1), 1.688(5); Fe–N(2), 1.678(6); Fe–N(3), 2.021(4); Fe–S(1), 2.2714(17); N(1)–O(1), 1.162(6); N(2)–O(2), 1.171(6); S(1)····N(5), 2.986; N(2)–Fe–N(1), 114.3(2); N(3)–Fe–S(1), 105.47(14); N(2)–Fe–N(3), 108.9(2); N(1)–Fe–N(3), 109.9(2); N(2)–Fe–S(1), 110.56(19); O(1)–N(1)–Fe(1), 166.0(5); O(2)–N(2)–Fe(1), 166.0(5).

The coordinated imidazole ligand of DNIC **2** could be replaced by thiolate $[SC_6H_4\text{-}o\text{-}NHCOPh]^-$. As shown in Scheme 1b, the reaction of DNIC **2** (0.042 g, 0.1 mmol) and 1 equiv of $[SC_6H_4\text{-}o\text{-}NHCOPh]^-$ (0.077 g, 0.1 mmol) in a THF solution at room temperature rapidly yielded the oily anionic $\{Fe(NO)_2\}^9$.

DNIC **3** (yield 0.109 g, 98%) is characterized by IR, UV–vis, and EPR.[9a,13] The [Fe(NO)$_2$] unit remains intact during the ligand exchange. The IR spectra for DNICs **2** and **3** had the same pattern but differed in the position (1722 and 1786 cm^{-1} for **2** versus 1705 and 1752 cm^{-1} for **3**) and separation of NO stretching frequencies ($\Delta\nu_{NO}$ = 64 cm^{-1} for **2** versus 47 cm^{-1} for **3**). In contrast, DNIC **3** does not react with imidazole to yield DNIC **2**. This result shows that the

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(12) Complex **2**. IR (ν_{NO}): 1722 s, 1786 s (THF) cm^{-1}. Absorption spectrum (CH$_2$Cl$_2$) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})]: 378 (5091), 450 (2000), 787 (319). Anal. Calcd for $C_{16}H_{14}O_3SN_5Fe$: C, 46.62; H, 3.42; N, 16.99. Found: C, 47.02; H, 3.60; N, 16.80.

(13) Complex **3**. IR (ν_{NO}): 1705 s, 1752 s (THF) cm^{-1}. Absorption spectrum (THF) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})]: 460 (1312), 785 (236).

thiolate-coordinated ligands of complex **3** promote the stability of the $\{Fe(NO)_2\}^9$ DNICs compared to the neutral imidazole-coordinated ligand. Compared to the well-resolved nine-line EPR spectrum of DNIC **2** with $g = 2.031$, complex **3** exhibits a well-resolved five-line EPR spectrum with a signal at $g = 2.029$, the characteristic g value of DNICs,[1−5] and a hyperfine coupling constant of 2.344 G at 298 K (Figure 1b).[9a] Protonation (HBF_4, 0.2 mmol) of DNIC **3** (0.222 g, 0.2 mmol) is presumed to occur only at the more accessible, electron-rich S site to form the well-known complex **1** (0.103 g, 95%) at ambient temperature (Scheme 1c). Reversibly, quantitative transformation of complex **1** to **3** was monitored by IR ν_{NO} spectra; the shift of the stretching frequencies from 1759 and 1787 cm^{-1} to the lower wavenumbers 1705 and 1752 cm^{-1} confirmed the formation of the anionic $\{Fe(NO)_2\}^9$ DNIC **3** (yield 83%) when a THF solution of the dinuclear complex **1** (0.138 g, 0.2 mmol) was reacted with 2 equiv of $[SC_6H_4\text{-}o\text{-}NHCOPh]^-$ (0.307 g, 0.4 mmol; Scheme 1c′). Obviously, DNIC **2**, Roussin's red ester **1**, and DNIC **3** are chemically interconvertible.

In summary, the facile interconversions among the neutral $\{Fe(NO)_2\}^9$ complex **2**, the anionic $\{Fe(NO)_2\}^9$ complex **3**, and Roussin's red ester **1** were demonstrated. The results obtained from this work also imply that the EPR spectrum (the pattern of hyperfine splitting) in combination with IR ν_{NO} (the relative position of the ν_{NO} stretching frequencies) spectrum may serve as an efficient tool for the discrimination of the existence of the anionic $\{Fe(NO)_2\}^9$ DNICs, the neutral $\{Fe(NO)_2\}^9$ DNICs, and Roussin's red ester.[14] We expect that the study of the anionic/neutral $\{Fe(NO)_2\}^9$ DNICs, and the interconversion of the anionic/neutral $\{Fe(NO)_2\}^9$ DNICs and Roussin's red ester, may predict/decipher the $\{Fe(NO)_2\}$ ligation of DNICs in the biological system.[14] Studies of the NO/Fe oxidation state(s) of this series of neutral $\{Fe(NO)_2\}^9$ DNICs by X-ray absorption spectroscopy and the influence of the $\{Fe(NO)_2\}^9$ electronic structure of the neutral DNICs on NO-releasing ability are ongoing.

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Supporting Information Available: X-ray crystallographic file in CIF format for the structural determination of **2**, experimental details, UV−vis, IR, and ^1H NMR spectra, crystallographic data and refinement parameters, and bond distances and angles. This material is available free of charge via the Internet at http://pubs.acs.org.

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