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COMMUNICATIONS

Published on Web 02/22/2006

Interaction of Nitric Oxide with Tetrathiolato Iron(II) Complexes: Relevance to the Reaction Pathways of Iron Nitrosyls in Sulfur-Rich Biological Coordination Environments

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Nitric oxide (NO) modulates a variety of physiological properties, including blood pressure, neurotransmission, and the immune response.[1−3] Some of the physiologically relevant chemistry of NO derives from its reactions with cysteine residues in proteins to generate nitrosothiols (RSNOs)[4] and with heme iron to form nitrosylated or S-nitrosated species.[5] Naturally occurring iron nitrosyls include four-coordinate, cysteine-ligated dinitrosyl iron complexes (DNICs)[6] proposed to form via NO-mediated iron−sulfur cluster degradation.[7] Interest in the mechanism of formation and properties of these dinitrosyls originates from the significant biological chemistry they transduce. DNICs have been suggested to be an alternative means of storing and transporting NO, like RSNOs, to generate such biological activity as vasodilation.[8] Additionally, DNICs have been implicated in the reduction of NO cytotoxicity[9] and are suggested as intermediates in the iron-catalyzed degradation and formation of S-nitrosothiols.[10] The lack of synthetic analogues to mimic the reactivity of DNICs[11] and other nitrosyl derivatives,[11c,12] in particular, their formation via the reaction of NO with iron−sulfur complexes, makes them especially interesting targets for study in bioinorganic chemistry. In this communication, we describe our first work in this area, namely, the synthesis, structural and spectroscopic characterization, and reactivity of an unprecedented four-coordinate mononitrosyl iron thiolate complex formed in the reaction of NO (g) with $(Et_4N)_2[Fe(S^tBu)_4]$.

When $(Et_4N)_2[Fe(S^tBu)_4]$ was allowed to react under anaerobic conditions with 1 mol-equiv of NO (g) in MeCN/THF (1:1) at −15 °C, a red−violet mononuclear tetrahedral iron−nitrosyl species, $(Et_4N)[Fe(S^tBu)_3(NO)]$ (**1**), was isolated in 74% yield. Addition of NO (g) to other $[Fe(SR)_4]^{2-}$ complexes (R = Ph or benzyl) under similar reaction conditions resulted only in the corresponding DNICs, irrespective of the amount of NO present. The more bulky *tert*-butyl alkyl groups are apparently required to isolate the mononitrosyl iron tris(thiolate) complex. Solutions of **1** are stable to vigorous Ar purging and vacuum, but extremely sensitive to air, water, and light, with somewhat greater stability in the solid state.

Dark-red X-ray quality crystals of **1** were obtained under anaerobic conditions by slow diffusion of pentane into a THF solution of the complex at −25 °C. The crystal structure revealed a four-coordinate iron center in a distorted tetrahedral geometry originating from three *tert*-butylthiolato-*S* ligands and one linearly coordinated NO molecule (Figure 1). The distortions at the metal center are most easily apparent from the bond angles about iron, which deviate from the 109.5° expected for a perfect tetrahedron (viz. S1−Fe1−S2, 116.138(17)° and N1−Fe1−S1, 103.22(4)°). The Fe−S distances are also somewhat variable as in other structurally characterized tetrathiolato Fe(III) complexes (vide infra).[13] The Fe−N(O) bond distance (1.7110(14) Å) is similar to those noted for other {Fe−NO}^{7} complexes,[11] but the nearly linear Fe−N−O bond angle is quite distinct from those in most characterized {Fe−NO}^{7} nitrosyls.[14] The existence of **1** suggests that similar

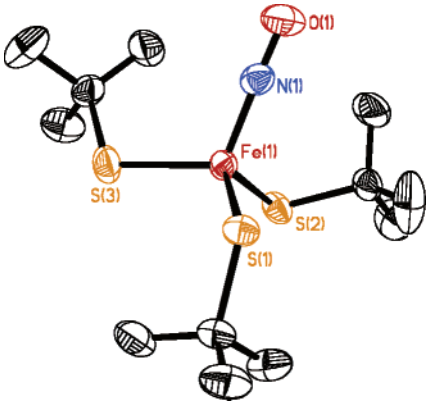

Figure 1. ORTEP diagram of the anion of $(Et_4N)[Fe(S^tBu)_3(NO)]$ (**1**) showing 50% thermal ellipsoids for all non-hydrogen atoms. Selected bond distances (Å) and angles (deg): Fe1−S1, 2.2885(4); Fe1−S2, 2.2639(4); Fe1−S3, 2.2686(5); Fe1−N1, 1.7110(14); N1−O1, 1.1677(19); Fe1−N1−O1, 174.18(13); N1−Fe1−S1, 103.22(4); S1−Fe1−S2, 116.138(17); N1−Fe1−S2, 109.21(5); N1−Fe1−S3, 113.22(5).

mononitrosyls may be important species traversed along the pathway to DNIC formation in biology.[15]

As noted above, we assign the nitrosyl complex **1**, according to the Enemark−Feltham notation,[16] as an {Fe−NO}^{7} species. In agreement with this formalism, its EPR spectrum at 4.2 K in a 1:1 CH_2Cl_2/toluene frozen solution exhibits *g*-values at 3.84, 3.16, and 2.01 consistent with an $S = {}^3/_2$ spin system.[17] The $S = {}^3/_2$ ground spin state of **1** was also established by variable temperature magnetic susceptibility measurements, which yielded $\mu_{eff} = 3.97 \pm 0.06\ \mu_B$ between 50 and 300 K. An $S = {}^3/_2$ value can arise either from high-spin Fe(II) antiferromagnetically coupled to NO or from high-spin Fe(III) antiferromagnetically coupled to NO^-. To probe further the nature of the oxidation state of the iron center in **1**, its Mössbauer spectrum was measured at 4.2 K. The observed isomer shift (δ) of 0.26(2) mm/s for **1** is consistent with a high-spin Fe(III) center in this coordination environment.[18] Oxidation to Fe(III) is also in agreement with the short Fe−S bond distances (av: 2.2737(4) Å), which are similar to those in $(Et_4N)[Fe(SEt)_4]$ (av: 2.269(1) Å).[13] The FTIR spectrum of **1** displays its ν_{NO} stretch at 1704 cm^{-1} (KBr matrix), which shifts to 1670 cm^{-1} upon isotopic substitution with ^{15}NO. The latter value agrees with that computed by assuming a classical diatomic oscillator, 1673 cm^{-1}. Although seemingly high for a formally NO^- ligand, a similar ν_{NO} stretch of 1692 cm^{-1} was observed for the {Fe−NO}^{7} compound [Fe(NO)(TC-5,5)], previously synthesized in our laboratory, which contains a linear Fe−N−O group and is proposed to contain coordinated NO^-.[14] Collectively, the physical data described above support the assignment of a high-spin Fe(III)−NO^- unit in **1**.

In contrast to the reactivity of **1** with NO (g), addition of $NOBF_4$ as an NO^+ source in MeCN resulted in the formation of the

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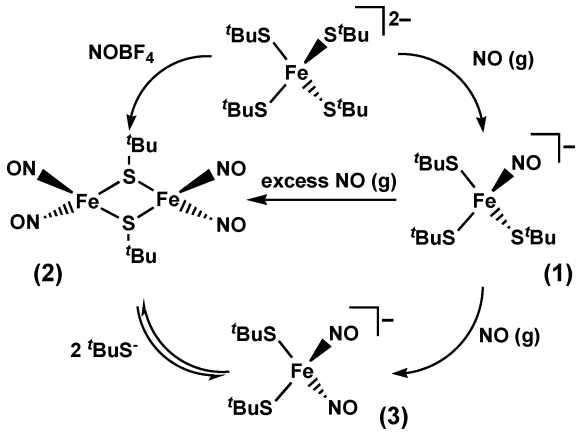
Scheme 1



dinuclear dinitrosyl Roussin red ester derivative, $[Fe_2(\mu\text{-}S^tBu)_2(NO)_4]$ (**2**). X-ray crystallographic analysis of red−brown **2** revealed that the Fe−N(O) and N−O distances (av: 1.6676(14) and 1.1685(19) Å, respectively) differ only slightly from those observed in **1**.[19] The Fe−N−O angles are slightly more bent in **2**, 169.01(14)°, than in the mononitrosyl **1**. The dinitrosyl species is easily distinguished by its IR spectrum (ν_{NO} = 1729 and 1778 cm^{-1} in KBr). In contrast to **1**, complex **2** is diamagnetic as a result of the coupling of unpaired electrons between the two $\{Fe(NO)_2\}$ units.

The nitrosyl complexes **1** and **2** can be chemically converted to the DNIC $[Fe(S^tBu)_2(NO)_2]^-$ (**3**) (Scheme 1), as monitored by following their characteristic UV−vis, EPR, and FTIR spectra.[11c] Addition of a stoichiometric quantity of NO (g) to $[Fe(S^tBu)_4]^{2-}$ to yield **1** is clean and involves only ligand displacement of one *tert*-butylthiolato-*S* ligand by one NO, as evidenced in the formation of $(Et_4N)(S^tBu)$ by ^1H NMR spectroscopy, with no change in the overall redox state of the complex. Addition of one more equivalent of NO (g) results in conversion of **1** into its DNIC analogue **3**, formed by two-electron reduction of **1** with concomitant generation of the disulfide ^{t}BuSS^{t}Bu. Passage of excess NO (g) through an MeCN solution of **1** affords the Roussin ester **2**. Conversion of the dinuclear complex **2** into DNIC **3** can also be readily achieved by addition of excess ^{t}BuS$^-$ to an MeCN solution of **2**.

In conclusion, we have successfully isolated and structurally characterized a four-coordinate non-heme mononitrosyl species **1** and its analogous dinuclear Roussin ester **2**. To the best of our knowledge, complex **1** is the first and only structurally characterized example of this type of iron−nitrosyl complex. Its existence suggests that similar mononitrosyls may be important species in the generation of DNICs in biology. Compounds such as **1** may also serve as efficient transport or delivery agents for biological NO, as has been suggested for DNICs, and its ability to transfer NO to heme groups has been established in preliminary studies in our laboratory. The nitrosyl complexes reported in this account can both convert to the corresponding DNIC, as shown in Scheme 1. Their spectroscopic (UV−vis, EPR, and FTIR) and structural properties, and the reaction chemistry that interconverts them, should aid in the identification of reactive species and pathways for nitrosylation of iron−sulfur sites in biology.

Acknowledgment. This work was supported by NSF Grant CHE-0234951. T.C.H. is a National Institutes of Health postdoctoral fellow (1 F32 GM075684-01). We thank Ms. Mi Hee Lim and Mr. Andrew G. Tennyson for helpful discussions.

Supporting Information Available: Experimental details for the synthesis of **1** and **2**, UV−vis, EPR, FTIR, and X-ray crystallographic data, including tables, ORTEP diagrams, and CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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JA060186N