

## RESEARCH ARTICLE

Thionitrite ( $\text{SNO}^-$ ) and Perthionitrite ( $\text{SSNO}^-$ ) are Simple Synthons for Nitrosylated Iron Sulfur ClustersTobias J. Sherbow,<sup>[a]</sup> Wen Fu,<sup>[b]</sup> Lizhi Tao,<sup>[b]</sup> Lev N. Zakharov,<sup>[a]</sup> R. David Britt,<sup>[b]</sup> and Michael D. Pluth<sup>\*[a]</sup>

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**Abstract:** S/N crosstalk species derived from the interconnected reactivity of  $\text{H}_2\text{S}$  and NO facilitate the transport of reactive sulfur and nitrogen species in signaling, transport, and regulatory processes. We report here that simple  $\text{Fe}^{2+}$  ions, such as those that are bioavailable in the labile iron pool (LIP), react with thionitrite ( $\text{SNO}^-$ ) and perthionitrite ( $\text{SSNO}^-$ ) to yield the dinitrosyl iron complex  $[\text{Fe}(\text{NO})_2(\text{S}_5)]^-$ . In the reaction of  $\text{FeCl}_2$  with  $\text{SNO}^-$  we were also able to isolate the unstable intermediate hydrosulfido mononitrosyl iron complex  $[\text{FeCl}_2(\text{NO})(\text{SH})]^-$ , which was characterized by X-ray crystallography. We also show that  $[\text{Fe}(\text{NO})_2(\text{S}_5)]^-$  is a simple synthon for nitrosylated Fe-S clusters via its reduction with  $\text{PPh}_3$  to yield Roussin's Red Salt ( $[\text{Fe}_2\text{S}_2(\text{NO})_4]^{2-}$ ), which highlights the role of S/N crosstalk species in the assembly of fundamental Fe-S motifs.

## Introduction

Small gaseous molecules that are endogenously produced and function on molecular targets play essential roles in physiological function. Canonical examples of these molecules, often referred to as gasotransmitters, include CO, NO, and  $\text{H}_2\text{S}$  – each being derived from larger biomolecules through enzymatic processes.<sup>[1]</sup> The reaction between gasotransmitters and related species forms a landscape of intertwined reactive intermediates, or crosstalk species, that are postulated to facilitate different signaling, transport, and regulatory processes. Thionitrous acid ( $\text{HSNO}$ ) is the simplest S/N crosstalk species and is formed from the direct reaction of S-nitrosothiols ( $\text{RSNO}$ ) with  $\text{H}_2\text{S}$ . Filipovic and coworkers demonstrated that  $\text{HSNO}$  is membrane permeable and facilitates protein transnitrosation via the transport and subsequent generation of  $\text{NO}^+$  and  $\text{HS}^-$  equivalents.<sup>[2]</sup> Work from Feelisch and coworkers demonstrated that aerobic oxidation of  $\text{H}_2\text{S}$  and NO results in the intermediate generation of  $\text{HSNO}$  and polysulfides en route to formation of perthionitrite ( $\text{SSNO}^-$ ), which functions as a source of bioavailable sulfane sulfur, polysulfides, and NO.<sup>[3]</sup> Furthermore, these results cement that the generation of crosstalk species from  $\text{H}_2\text{S}$  and NO requires the presence of oxidants.

Gasotransmitter uptake, regulation, and transport is also intertwined with bioinorganic metal centers. For example, NO binds and activates heme in soluble guanylate cyclase to rapidly produce cyclic guanosine monophosphate (cGMP) and generates a physiological response, such as muscle relaxation.<sup>[4]</sup> Ferric hemoglobin can bind and oxidize hydrosulfide to thiosulfate and

iron-bound hydropersulfides, which are crucial reactive sulfur species (RSS) formed in persulfidation signaling pathways.<sup>[5]</sup> Despite the demonstrated ability of iron systems to interact with NO and  $\text{H}_2\text{S}$ , surprisingly few studies have investigated how metals participate in the generation and interconversion S/N crosstalk species.

Both  $\text{SNO}^-$  and  $\text{SSNO}^-$  can bind to Lewis acidic redox inert metals with potential coordination to S, N, or O. Recent work from Warren and coworkers demonstrated that salt metathesis of redox inert  $\text{TpZn}(\text{ClO}_4)$  ( $\text{Tp}$  = hydrotris(5-methyl-3-phenylpyrazol-1-yl)borate) with  $\text{SSNO}^-$  efficiently formed  $\text{TpZn}(\kappa^2\text{-SSNO})$ , which was fully characterized.<sup>[6]</sup> Subsequent abstraction of one sulfane sulfur atom from  $\text{TpZn}(\kappa^2\text{-SSNO})$  with  $\text{PET}_3$  formed  $\text{TpZn}(\text{SNO})$  in high yield. Both  $\text{TpZn}(\kappa^2\text{-SSNO})$  and  $\text{TpZn}(\text{SNO})$  were stable at room temperature and decomposed to release NO at elevated temperature. Reaction of aryl thiols with  $\text{TpZn}(\kappa^2\text{-SSNO})$  or  $\text{TpZn}(\text{SNO})$  resulted in decomposition and release of NO and  $\text{S}_8$  via  $\text{HSSNO}$  formation, or  $\text{N}_2\text{O}$  and  $\text{S}_8$  via  $\text{HSNO}$  formation, respectively. Examples of  $\text{SNO}^-$  and  $\text{SSNO}^-$  coordination at biologically relevant redox-active metals remain unsurprisingly elusive, in part due to the redox instability of S/N crosstalk species. As an example of this complexity, reactions of sodium nitroprusside,  $\text{Na}_2[\text{Fe}(\text{CN})_5\text{NO}]$  (SNP), with hydrosulfide ( $\text{HS}^-$ ) have been studied for nearly 180 years,<sup>[7]</sup> but the products remained unknown until recently. Wu and coworkers characterized reactive intermediates by NMR ( $^{17}\text{O}$ ,  $^{15}\text{N}$ ,  $^{13}\text{C}$ ), UV-vis, and IR spectroscopy together with DFT calculations to show that SNP reacts with  $\text{HS}^-$  to form  $[\text{Fe}(\text{CN})_5(\text{SNO})]^{4-}$ , which can subsequently react with  $\text{HSS}^-$  to form  $[\text{Fe}(\text{CN})_5(\text{SSNO})]^{4-}$  with a distinct blue color ( $\lambda_{\text{max}} = 570 \text{ nm}$ )<sup>[8]</sup> Furthermore, related studies by Filipovic demonstrated that  $[\text{Fe}(\text{CN})_5(\text{SNO})]^{4-}$  can also be a source of  $\text{HNO}$ .<sup>[9]</sup> A separate example of  $\text{HS}^-$ -mediated nitrite reduction has been observed at a Fe-porphyrin (FeP) system and results in the formation of an FeP-NO complex, which can react with an additional equivalent of  $\text{HS}^-$  to form a FeP- $\text{HSNO}$  species that was characterized by cryospray ESI-TOF MS.

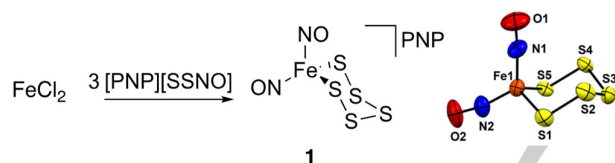
Expanding this coordination chemistry, an attractive hypothesis is that these pools of S/N crosstalk species may also be important synthons in the assembly of fundamental bioinorganic building blocks, particularly those with S and NO motifs. For example, mononitrosyl and dinitrosyl iron complexes (MNICs and DNICs, respectively) are prototypical Fe-NO species that have wide ranging functions including reducing oxidative stress,<sup>[10]</sup> repairing and/or degrading Fe-S clusters,<sup>[11]</sup> and signaling via protein S-nitrosation.<sup>[12]</sup> More broadly, the cellular

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labile iron pool (LIP), which consists of a chelatable pool of redox-active Fe ions,<sup>[13]</sup> is key in the formation of Fe-NO species and often proceeds through the initial generation of MNICs followed by subsequent reaction with thiols to generate DNICs.<sup>[14]</sup> The role of the LIP in sulfur metabolism may also result in formation of S/N crosstalk species, although the fundamental reactions of simple Fe species with like SNO<sup>-</sup> and SSNO<sup>-</sup> remains uninvestigated. Here we report that the simple reaction of SNO<sup>-</sup> and SSNO<sup>-</sup> with Fe<sup>2+</sup> generates MNIC and DNIC compounds, as well as NO, hydrosulfide, and persulfide equivalents, all of which highlight the role of S/N crosstalk species in the assembly of fundamental Fe-S motifs.

## Results and Discussion

Building from the idea that S/N crosstalk species could react with simple Fe sources, we investigated whether FeCl<sub>2</sub> could react directly with [PNP][SSNO]. Stirring FeCl<sub>2</sub> with 3 equiv of [PNP][SSNO] in THF led to an immediate color change from a colorless to a dark brown slurry, which became a homogenous dark brown solution after stirring for 24 h. Removal of the solvent under reduced pressure and recrystallization at -25 °C from a concentrated THF solution layered with hexane yielded the DNIC [PNP][Fe(NO)<sub>2</sub>(S<sub>5</sub>)] (**1**) (61%, with respect to Fe) as dark brown/blue crystals (Scheme 1).<sup>[15]</sup>



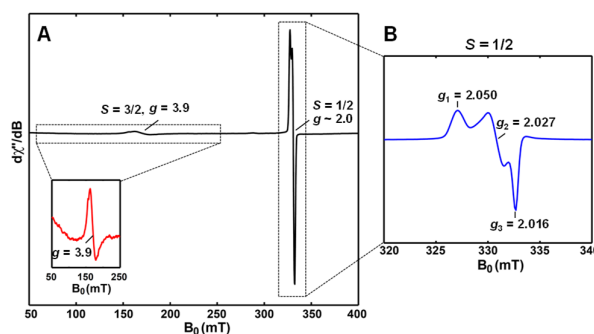
**Scheme 1.** Synthesis of complex **1** from FeCl<sub>2</sub> and [PNP][SSNO]. Solid state structure of [Fe(NO)<sub>2</sub>(S<sub>5</sub>)]<sup>-</sup> in **1**. Ellipsoids are shown at 50% probability levels. Blue, red, orange, and yellow ellipsoids represent N, O, Fe, and S atoms, respectively. The [PNP]<sup>+</sup> cation is omitted for clarity.

DNIC **1** shows two NO stretches in the IR spectrum at 1735 cm<sup>-1</sup> and 1685 cm<sup>-1</sup> (Table 1), which match previously published data for [Fe(NO)<sub>2</sub>(S<sub>5</sub>)]<sup>-</sup>.<sup>[16]</sup> We confirmed the molecular structure of **1** using single crystal X-ray diffraction (Scheme 1, Table S1). The prior reported synthesis of **1** relied on the direct reaction of the MNIC [PNP][Fe(CO)<sub>3</sub>(NO)] with S<sub>8</sub>, which generates **1** in only 45% yield (based on total Fe) due to formation of a [PPN]<sub>2</sub>[S<sub>5</sub>Fe(μ-S)<sub>2</sub>FeS<sub>5</sub>] byproduct. In the reaction of FeCl<sub>2</sub> with [PNP][SSNO], we did not detect any other Fe containing byproducts, and highlights the efficiency of forming polysulfide-based DNICs from SSNO<sup>-</sup> and Fe<sup>2+</sup>.

**Table 1.** Selected Bond Lengths, Angles and Vibrational Stretches for Compounds 1-3.

	1	2	3
<(Fe-N-O) (°)	172.9(2), 166.2(3)	170.0(6)	171.8(2), 163.1(2)
d(N-O) (Å)	1.166(3), 1.174(3)	1.140(7)	1.181(3), 1.187(3)
d(Fe-N) (Å)	1.670(2), 1.683(2)	1.731(5)	1.663(2), 1.681(2)
ν <sub>N-O</sub> (cm <sup>-1</sup> )	1735, 1685	1795	1650, 1618
r <sub>4</sub> <sup>[17][18]</sup>	0.92	0.98	0.99

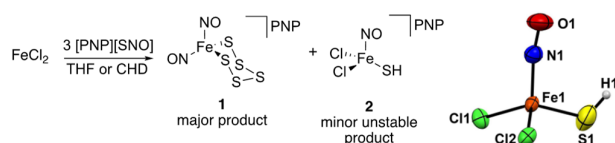
Based on the polysulfide backbone of **1**, we next investigated the reaction of FeCl<sub>2</sub> with [PNP][SNO] to determine the reaction outcome when sulfane sulfur sources were removed from the reaction. We treated FeCl<sub>2</sub> with 3 equiv of [PNP][SNO] in THF, which led to an immediate color change from a colorless to a dark brown slurry, and became homogenous after 24 h. The solvent was removed under reduced pressure, and excess [PNP][SNO] was removed from the brown residue by extraction with benzene. We analyzed the resultant reaction products by IR spectroscopy, EPR spectroscopy, Evan's Method magnetic susceptibility, and X-ray diffraction studies. IR spectra of the brown residue were acquired (Figure 2) and showed NO stretches at 1735 cm<sup>-1</sup> and 1685 cm<sup>-1</sup>, which matched that of complex **1** as well as a new, but weak NO stretch observed at 1795 cm<sup>-1</sup>. The presence of a new NO stretch suggested that more than one Fe-NO containing product was formed. From the IR data we concluded that the major product in the reaction is complex **1** and the minor product is a new complex (*vide infra*, complex **2**). This assignment was further confirmed from EPR spectroscopy on the reaction mixture. Crystalline samples from the reaction between FeCl<sub>2</sub> and SNO<sup>-</sup> were dissolved in 1:1 toluene/THF and flash frozen in liquid nitrogen. The frozen-solution state EPR spectrum was then recorded at 10 K, as shown in Figure 1. Two paramagnetic components were observed, where a major component is an S = 1/2 species with g-values = [2.050, 2.027, 2.016] at central field and a minor component at low-field with g ~ 3.9 is consistent with a high spin S = 3/2 species.<sup>[19]</sup> The major component is assigned to **1**, because the corresponding electronic spin states (low-spin S = 1/2 and g-values match those of **1** previously reported by Tsai et al.<sup>[16]</sup> Evan's method magnetic susceptibility measurements from crystalline samples from the reaction between FeCl<sub>2</sub> and SNO<sup>-</sup> showed μ<sub>eff</sub> = 2.10 μ<sub>B</sub>. This μ<sub>eff</sub> value is slightly higher than that of a pure sample consisting of an S = 1/2 system, which is consistent with some incorporation of an S = 3/2 product. These data also corroborates the EPR results that both S = 1/2 and S = 3/2 species were detected from the crystalline sample.



**Figure 1.** X-band (9.38 GHz) continuous-wave (CW) EPR spectra (10 K) of frozen-solution crystalline samples from the reaction between FeCl<sub>2</sub> and SNO<sup>-</sup> in 1:1 toluene/THF. (A) A full-spectrum shows both S = 3/2 and S = 1/2 signals recorded at 10 K, with 6.325 mW microwave power (non-saturating for S = 3/2 signal). (B) A non-saturating signal for the S = 1/2 species obtained by recording the spectrum at 10 K using a much lower microwave power (0.0006325 mW).

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Further analysis of these products was performed using X-ray crystallography. Single crystals from the reaction of  $\text{FeCl}_2$  and  $\text{SNO}^-$  grown at  $-25^\circ\text{C}$  from a concentrated THF solution layered with hexane and afforded two types of crystals. X-ray diffraction studies of two separate crystals confirmed the molecular structures of two products as **1** and  $[\text{PNP}][\text{Fe}(\text{NO})(\text{SH})\text{Cl}_2]$  (**2**) (Scheme 2). The formation of both **1** and **2** was reproducible based on unit cell determinations from replicate reactions and different batches of crystals. Crystalline **2** appears as an almost black solid to the naked eye, but has a deep blue tint when examined under a microscope. Complex **2** is a tetrahedral monoanionic Fe complex with a  $\tau_4$  value of 0.98, consisting of two anionic chloride, one NO, and one  $\text{HS}^-$  ligand. Complex **2** is therefore assigned to the  $S = 3/2$  species observed in the EPR spectrum. We note that **2** is unstable and readily decomposes at room temperature.

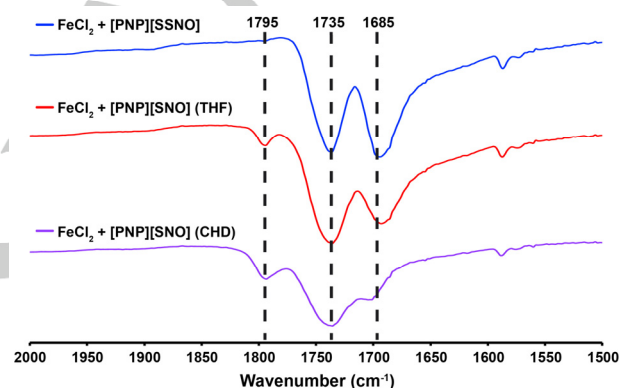


**Scheme 2.** Products isolated from the reaction of  $\text{FeCl}_2$  and  $[\text{PNP}][\text{SNO}]$ , including the solid state structure of  $[\text{Fe}(\text{NO})(\text{SH})\text{Cl}_2]^-$  in **2**. Ellipsoids are shown at 50% probability levels. White, blue, red, green, orange and yellow ellipsoids represent H, N, O, Cl, Fe and S atoms, respectively. The  $[\text{PNP}]^+$  cation is omitted for clarity.

Based on the observation but instability of **2**, we hypothesize that **2** is a potential reactive intermediate in the formation of DNIC **1**. The intermediate formation of MNICs en route to DNIC formation is also consistent with biological DNIC formation from the LIP.<sup>[14, 20]</sup> To the best of our knowledge, MNIC **2** is one of only six other hydrosulfidonoritrosyl metal complexes<sup>[21]</sup> that have been structurally characterized and the only example of a structurally characterized mononuclear MNIC containing an  $\text{HS}^-$  ligand. We did not observe a  $\nu_{\text{S-H}}$  stretch in **2**, but the absence of M-SH stretches is relatively common for otherwise fully-characterized M-SH species.<sup>[22]</sup> We are aware that SH and Cl can be difficult to distinguish crystallographically, however the structural data supports the assignment of **2** as  $[\text{Fe}(\text{NO})(\text{SH})\text{Cl}_2]^-$ . The sulfhydryl hydrogen of the Fe-SH motif in **2** was located in the residual density map and refined without restrictions. Furthermore, the Fe-Cl and Fe-SH distances vary in the molecule, with the two Fe-Cl distances being identical (2.2399(16) Å, 2.2411(16) Å) and the Fe-S distance being shorter (2.203(2) Å). When compared to other tetrahedral  $\text{Fe}(\text{NO})\text{-Cl}$  complexes, the Fe-Cl distances in **2** are similar compared to the  $[\text{Fe}(\text{NO})\text{Cl}_3]^-$  anion which has Fe-Cl distances between 2.2207(11) Å and 2.2340(9) Å.<sup>[23]</sup> The Fe-SH distance of 2.203(2) Å in **2** is in the lower quartile Fe-SH bonds distances.<sup>[22]</sup> The coordination environment of **2** is consistent with an  $\{\text{FeNO}\}^7$  electronic structure using Enemark-Feltham notation.<sup>[24]</sup> The Fe-N-O bond angle, Fe-N<sub>NO</sub>, N-O bond length, and  $\nu_{\text{N-O}}$  in **2** are 170.0(6)°, 1.731(5) Å, 1.140(7) Å, and 1795  $\text{cm}^{-1}$ , respectively, and are consistent with other  $\text{Fe}^{\text{III}}\text{-NO}^-$  electronic structures,<sup>[25]</sup> where the triplet  $\text{NO}^-$  is antiferromagnetically coupled to the high-spin  $\text{Fe}^{\text{III}}$ .

Based on the isolation of **2**, we propose that formation of **1** proceeds through coordination of  $\text{SNO}^-$  followed by rapid

homolytic cleavage of the S-N bond to provide a NO ligand and a transient thiyl radical (*vide infra*). The homolytic cleavage pathway of  $\text{SNO}^-$  has been observed previously in the generation of NO and polysulfides from  $\text{HSNO}$ .<sup>[2]</sup> Furthermore, thiyl radicals are known to facilitate hydrogen atom transfer reactions to form thiols,<sup>[26]</sup> which should result in hydrosulfide generation in this system.<sup>[27]</sup> Based on the proposed mechanism involving a thiyl radical to form the hydrosulfide ligand in **2**, we added 1,4-cyclohexadiene (CHD), which contains a weak C-H bond, to determine whether the yield of **2** could be increased. We repeated the reaction between  $\text{FeCl}_2$  and  $\text{SNO}^-$  in the presence of excess CHD in THF following the previous procedure. The IR spectrum of the reaction product was compared to that of the same reaction in the absence of CHD and also the reaction of  $\text{FeCl}_2$  with  $[\text{PNP}][\text{SSNO}]$  where only complex **1** is formed (Figure 2). The resultant IR data suggest that addition of CHD results in more formation of **2**, which further supports the intermediacy of a thiyl radical.

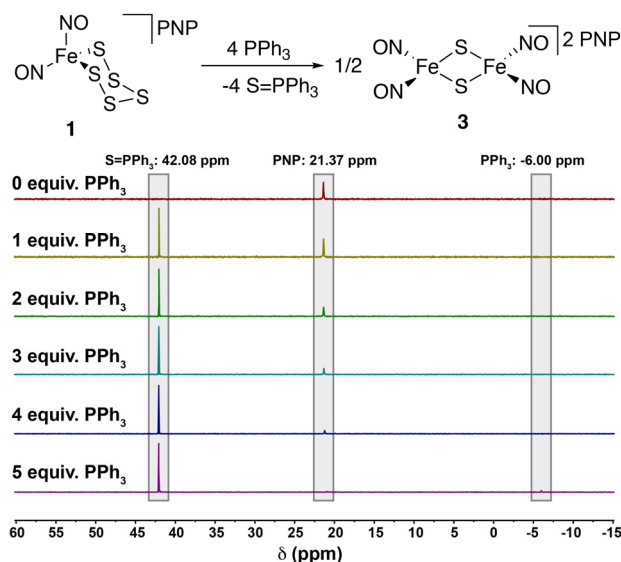


**Figure 2.** Partial IR spectra of the NO stretching frequency region of the reaction between (top, blue)  $\text{FeCl}_2$  with  $[\text{PNP}][\text{SSNO}]$  yielding  $[\text{Fe}(\text{NO})_2(\text{S}_3)]^-$ , (middle, red)  $\text{FeCl}_2$  with  $[\text{PNP}][\text{SNO}]$  in THF yielding a mixture of  $[\text{FeCl}_2(\text{NO})(\text{SH})]^-$  and  $[\text{Fe}(\text{NO})_2(\text{S}_3)]^-$ , and (bottom, purple)  $\text{FeCl}_2$  with  $[\text{PNP}][\text{SNO}]$  in CHD yielding a mixture of  $[\text{FeCl}_2(\text{NO})(\text{SH})]^-$  and  $[\text{Fe}(\text{NO})_2(\text{S}_3)]^-$ . The NO stretches at 1735  $\text{cm}^{-1}$  and 1685  $\text{cm}^{-1}$  correspond to complex **1** and we assign the NO stretch at 1795  $\text{cm}^{-1}$  to complex **2**.

To further expand the connection of S/N crosstalk species with Fe-S building blocks, we next investigated whether polysulfide-based DNICs, such as **1**, can function as precursors to form biologically-relevant nitrosylated Fe-S components. Because **1** contains up to four sulfane sulfur equivalents, we expected that these  $\text{S}^0$  atoms could be extracted using a mild reducing agent.<sup>[6, 28]</sup> Addition of one equiv of  $\text{PPh}_3$  to **1** resulted in a new resonance in the  $^{31}\text{P}$  NMR spectrum at 42.08 ppm, which corresponded to  $\text{S}=\text{PPh}_3$ . No resonance corresponding to free  $\text{PPh}_3$  were observed, which supports that all of the  $\text{PPh}_3$  had been consumed and that the reduction reaction was rapid (Figure 3). Continued sequential additions of up to four equiv of  $\text{PPh}_3$  resulted in complete conversion from  $\text{PPh}_3$  to  $\text{S}=\text{PPh}_3$  and the formation of a red-brown precipitate in the solution. The addition of a fifth equiv of  $\text{PPh}_3$  showed no further conversion to  $\text{S}=\text{PPh}_3$ , and a  $\text{PPh}_3$  resonance at -6.00 ppm was observed suggesting that all sulfane sulfur in the reaction mixture had been reduced. The resultant red-brown precipitate formed during the reaction was filtered and isolated. Two NO stretches were observed by IR

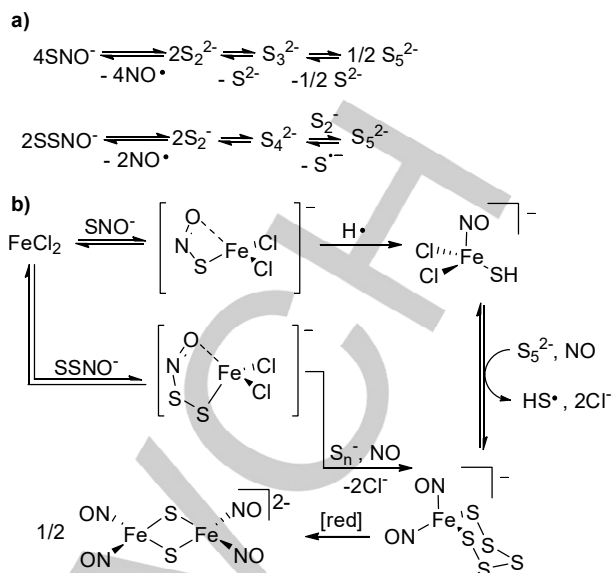
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spectroscopy at 1650  $\text{cm}^{-1}$  and 1618  $\text{cm}^{-1}$ , which matches those of Roussin's Red Salt (RRS). To verify the formation of RRS, a single crystal of the reaction product was grown from a concentrated MeCN solution layered with  $\text{Et}_2\text{O}$ . The molecular structure obtained by X-ray crystallography confirmed formation of RRS  $[\text{PNP}]_2[\text{Fe}(\text{NO})_2(\mu\text{-S})_2]$  (**3**) (Scheme 3, Figure S1, Table S1). Taken together, these results highlight that  $\text{Fe}^{2+}$  and  $\text{SSNO}^-$  can be used to generate fundamental precursors to biomimetic nitrosylated iron sulfur clusters.



**Figure 3.**  $^{31}\text{P}\{^1\text{H}\}$  NMR spectra of the titration of complex **1** with  $\text{PPh}_3$  in  $\text{C}_6\text{D}_6$ . The  $[\text{PNP}]^+$  signal decreases overtime as the product precipitates out of solution.

With both the observed formation of DNIC **1** from  $\text{Fe}^{2+}$  and  $\text{SSNO}^-$  and  $\text{SNO}^-$ , as well as observation of MNIC **2** from  $\text{SNO}^-$  we propose that both  $\text{SSNO}^-$  and  $\text{SNO}^-$  initially coordinate to the metal center, followed by rapid homolytic cleavage of the S–N bond to provide a NO ligand and a transient  $\text{S}_2^{2-}$  polysulfide in the case of  $\text{SSNO}^-$  and a thyl radical and **2** in the case of  $\text{SNO}^-$  (Scheme 3). For  $\text{SNO}^-$ , subsequent reaction with NO and polysulfides formed through  $\text{SNO}^-$  disproportionation would lead to formation of **1**. Similarly, for  $\text{SSNO}^-$ , the released polysulfide after initial reaction with  $\text{Fe}^{2+}$  can result in further polysulfide formation and NO generation, both of which are required to form **1**. Prior work has demonstrated that  $\text{SSNO}^-$  can equilibrate to form polysulfides and free  $\text{NO}$ ,<sup>[29]</sup> and similarly  $\text{SNO}^-$  has been demonstrated to be a source of thyl radicals (that can recombine to yield polysulfides) and free NO. Taken together, both of these proposed mechanisms highlight that these hybrid S/N crosstalk species constitute key building blocks for assembly of more complex nitrosylated Fe–S motifs.



**Scheme 3.** a) Equilibria showing the formation of polysulfides and NO from  $\text{SSNO}^-$  and  $\text{SNO}^-$ . b) Proposed mechanism for the formation of complexes **1**, **2**, and **3** from  $\text{SNO}^-$  and  $\text{FeCl}_2$ .

## Conclusion

Both  $\text{Fe}^{2+}$  and  $\text{SSNO}^-$  are bioavailable bioinorganic building blocks, and we have demonstrated that these two species react to form simple DNIC **1**. Upon reduction with  $\text{PPh}_3$ , **1** is readily converted to biologically-relevant Fe–S cluster RRS. The reaction of  $\text{FeCl}_2$  with  $\text{SNO}^-$  also leads to the formation of **1**, but in this case a highly unstable and uncommon hydrosulfidonitrosyl intermediate **2** was observed and structurally characterized. The proposed mechanism for this transformation leverages the ability of  $\text{SNO}^-$  to form NO, polysulfides, and other sulfide species that can react to form both complexes **1** and **2**. The formation of MNIC and DNIC compounds from S/N hybrid species suggests that these anions may play a yet unappreciated role as efficient sulfidating and nitrosylating agents in the LIP and further highlights that  $\text{SNO}^-$  and  $\text{SSNO}^-$  may function as synthons for Fe–S clusters and related nitrosylated products.

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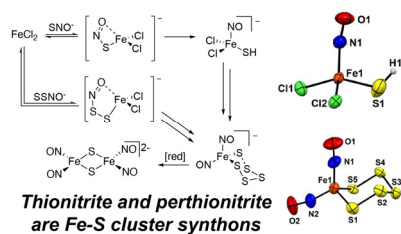
**Keywords:** reactive sulfur species • iron nitrosyl • thionitrite • per thionitrite

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## Entry for the Table of Contents



Simple Fe<sup>2+</sup> ions, such as those that are bioavailable in the labile iron pool, react with thionitrite (SNO<sup>-</sup>) and perthionitrite (SSNO<sup>-</sup>) to yield synthons to biologically-relevant Fe-S clusters.

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