Stabilizing Sulfur: Synthesis of a Terminal Fe^{III}=S Complex

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Summary: In this issue of *Chem*, Smith and coworkers describe the synthesis of a terminal iron-sulfide complex. FeS clusters are widespread cofactors in Nature, and this complex enables the study of the fundamental building block of such clusters and its comparison to more widely known terminal iron-oxo species.

Iron-sulfur (FeS) proteins are ubiquitous in Nature, being present in all forms of life from the most evolutionarily primitive to the most complex.[1] Indeed, some hypothesize that iron-sulfur minerals may have been responsible for early carbon-carbon bond forming reactions during the emergence of life on earth.[2] Well over 100 different types of enzymes containing FeS clusters are known and, the radical SAM (SAM = S-adenosylmethionine) superfamily alone contains over 700,000 unique enzymes, all of which depend on a 4Fe4S cluster for function.[3] The myriad roles of iron-sulfur proteins include a broad range of electron transfer reactions as well as some of the most challenging chemical transformations carried out by natural systems, including the fixation of atmospheric dinitrogen, carbon skeletal rearrangements and the modification of strong bonds in the synthesis of complex organic molecules. In fact, FeS clusters are critical to the protein assembly machinery responsible for the synthesis of the complex FeS active sites in other proteins, including nitrogenase (e.g. the FeMo cofactor, Figure 1A) and FeFe hydrogenase.[4]

In addition to biochemical investigations into the detailed structure, function, and mechanism of FeS proteins, synthetic chemistry has contributed significantly to our understanding of this class of cofactors through the preparation of model complexes of FeS cluster active sites.[5] Given the weak-field nature of the sulfide ligand and the tetrahedral geometry of the Fe centers, the Fe sites in biological FeS clusters are frequently high-spin, with complex magnetic interactions between the individual Fe centers leading to densely packed ladders of excited states accessible at room temperature and frequent paramagnetism. The complexity of both the electronic and molecular structures of FeS cofactors thus render them particularly challenging to study, especially in the context of a protein superstructure. To wit: the interstitial atom of the catalytic FeMo cofactor in nitrogenase (Figure 1A) was only definitively identified as carbon within the past 15 years.[6] Biological FeS clusters are most commonly found in 2Fe2S, 3Fe4S, 4Fe4S, although there are important higher nuclearity cofactors such as the FeMo-cofactor of nitrogenase (Figure 1A). In the 1970s, pioneering studies by Holm and coworkers revealed that a number of structurally and spectroscopically faithful analogues of biologically relevant FeS clusters were available to molecular synthetic chemistry apart from any macromolecular scaffold (Figure 1B).[7] Given the ability to rapidly modify these synthetic systems and characterize them via a range of atomically precise techniques, their study has aided significantly in understanding FeS cofactors in more complex protein environments.

Although molecular synthetic FeS cluster chemistry has been a thriving area of research for over five decades, very little is known about the fundamental unit of such clusters, $[Fe{=}S]^{n+}$ (Figure 1C) Such species have not been detected in biological systems, and the only known synthetic

example features extensive stabilization of the sulfide ligand via hydrogen bonding.[8] Smith and coworkers have previously utilized sterically demanding tris(carbene)borate ligands to stabilize terminal oxo, nitrido, and imido (=NR) complexes of Fe, and in this issue, they report the extension of this strategy to the synthesis of a terminal sulfide of Fe^{3+} absent any secondary stabilizing interactions of the sulfido ligand.[9] By treating an iron(I) dinitrogen complex with elemental sulfur, they achieve oxidative sulfur atom transfer to iron resulting in the Fe(III) sulfide. The steric bulk of the ligand serves to preclude the formation of Fe–S–Fe bridging interactions, and its anionic charge and the chelating configuration of the strongly coordinating carbene ligands serve prevent ligand dissociation and subsequent decomposition.

The unprecedented [Fe=S] complex was structurally characterized by single-crystal X-ray diffraction (SCXRD), revealing a trigonally symmetric four-coordinate complex with an Fe=S linkage of 2.1173(9) Å and confirming the absence of any stabilizing hydrogen bonding interactions with the sulfido ligand. The complex is relatively stable in solution, persisting for a significant time at –35 ºC, although decomposition is observed at room temperature over the course of 24 hours. This kinetic stability enabled the spectroscopic characterization of the complex by a range of spectroscopic techniques, including resonance Raman, Mössbauer, and electron paramagnetic resonance (EPR) spectroscopies. The resonance Raman spectra (407 nm excitation) reveals a strong band at a Raman shift of 470 cm^{-1}, consistent with a terminal Fe=S linkage. The ^{57}Fe Mössbauer spectrum of the Fe=S complex contains an asymmetric quadrupole doublet with an isomer shift of 0.24 mm/s, significantly different from the formally isoelectronic oxo and imido complexes supported by similar tris(carbene)borate ligands that feature isomer shifts of –0.15 and –0.11 mm/s, respectively. Both the oxo and imido complexes adopt low-spin, $S = ½$ ground states, and the discrepancy in the isomer shift of the related sulfido complex suggests that it instead adopts a high-spin ($S = 5/2$) configuration. This observation is remarkable given the strongly donating carbene supporting ligands and the anticipated π-bonding of the sulfido ligand. Low-temperature (12 K) EPR spectroscopy of the complex reveals an axial signal with apparent g-values of 6.50, 5.50, and 2.00, consistent with a high-spin Fe^{3+} center, and a measured magnetic moment of 5.8 μ_B at 298 K further supports the persistence of this high-spin state at room temperature.

Given the unusual electronic structure indicated by the spectroscopic experiments above, quantum chemical calculations were employed to further elucidate the bonding in the unprecedented Fe=S complex. Density functional theory (DFT) calculations of the complex in all plausible spin states ($S = ½$, 3/2, and 5/2) confirm the stability of the $S = 5/2$ state. Despite the partial occupation of all five d-orbitals, the authors note that this does not necessarily preclude the presence of significant Fe=S multiple bonding. Indeed, multireference complete active space self-consistent field (CASSCF) calculations accurately reproduce the Mössbauer parameters observed for the compound and indicate a dominant S = 5/2 configuration (86%). Inspection of the resulting orbital manifold confirms the presence of a filled σ-bonding orbital and two filled π-bonding orbitals between the Fe and S atoms. These interactions are countered by half-filled orbitals of π-antibonding character, suggesting a qualitative bond order of 2, but in an unconventional configuration of one σ-bond and two half π-bonds. As a result, the sulfur atom is expected to house a non-trivial amount of unpaired spin.

This unusual electronic structure is born out in the reactivity of the Fe=S complex, which reacts with 0.5 equivalents of dihydroanthracene (DHA) to afford the corresponding Fe(II)–SH complex

resulting hydrogen atom transfer from DHA to the sulfido ligand (Figure 1D). According to a SCXRD study, this hydrosulfido complex features a significantly longer Fe–S distance of 2.309(2) Å. Magnetic moment determination supports a high-spin configuration for the Fe–SH complex as well–in this case, an $S = 2$ spin state corresponding to d^6 configuration of the Fe^{2+} center. A significant primary kinetic isotope effect is observed for the reaction ($k_H/k_D = 2.1$), consistent with direct H-atom transfer in or before the rate determining step.

In conclusion, Smith and coworkers report the synthesis, characterization, and reactivity of the first example of a terminal iron sulfide complex free from secondary stabilization by hydrogen bonding. The key strategy in this synthesis is the use of a sterically demanding ancillary ligand to shield the reactive Fe=S moiety. Remarkably, the iron center is high-spin ($S = 3/2$) in contrast to the isoelectronic oxo and imido analogues. Despite this unusual spin state, the authors show the compound possesses significant multiple bond character. Further, the Fe=S unit is capable of cleaving weak C–H bonds to afford the Fe(II)–SH species. Although stable terminal Fe=S species have not been observed in biological systems, such species may be relevant to the structural dynamism of FeS clusters now thought to be important to the catalytic function biological systems.[10]

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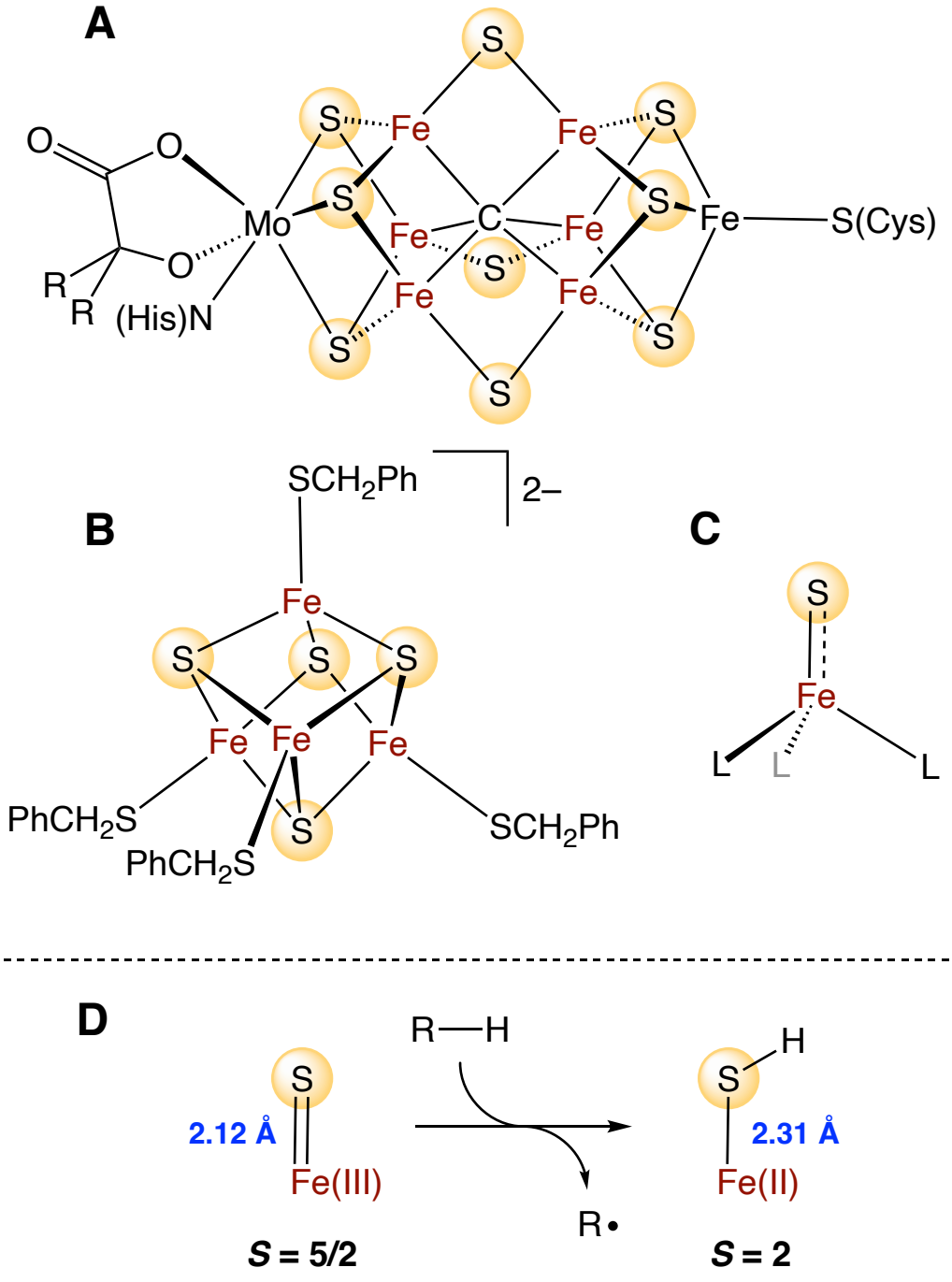

Figure 1. (A) The FeMo cofactor of nitrogenase; (B) a synthetic 4FeS4 cuboidal cluster; (C) a terminal Fe=S complex; (D) hydrogen atom transfer from a hydrocarbon to a terminal Fe(III)=S complex to yield a termina Fe(II)–SH complex. Fe–S bond lengths are indicated in blue.

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