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Synthesis of a $Fe^{II}SH$ Complex Stabilized by an Intramolecular N–H···S Hydrogen Bond, Which Acts as a H_2S Donor

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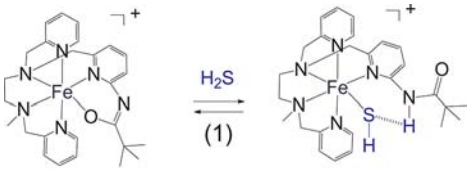
Supporting Information

ABSTRACT: Through use of the reversible protonation of an iron(II) complex containing a deprotonated carboxamido moiety, we prepared and fully characterized the first hydrogen(sulfido)iron(II) complex stabilized by an intramolecular hydrogen bond, which acts as a H_2S donor in solution.

Hydrogen bonding is a major noncovalent interaction, playing a key role as the structural determinant in many highly complex systems like proteins or DNA and in a wide range of catalytic reactions.[1] In metalloproteins, in addition to their structural role, hydrogen bonds can modulate the properties of the fragments coordinating a metallic cofactor. For example, in the case of cysteinyl ligands, hydrogen bonds have been proposed to impact the redox potential of iron–sulfur centers, as observed in rubredoxin[2] or in [2Fe–2S][3] and [4Fe–4S][4] clusters, or to account for the specific alkylation of one of the four cysteines bound to the zinc center in the ADA repair protein.[5] To clearly discriminate between the contribution of hydrogen-bonding interactions and other protein contributions like solvent accessibility or dielectric effects, these biochemical studies have been completed by the development of synthetic models containing hydrogen-bonded thiolato ligands. They have confirmed the importance of hydrogen bonds in the aforementioned systems[6] and have also provided new insight into the possible role of these interactions, like the protection of thiolato species from oxidation in superoxide dismutase related nickel complexes.[7] More recently, hydrogen sulfide has been shown to be a major biological player, in particular through its interactions with hemoproteins.[8] In these systems, hydrogen bonds are again essential for control of the affinity and redox activity of hydrogen sulfide. Indeed, the presence of a hydrogen-bond donor in the heme pocket stabilizes the bound hydrosulfide ligand HS^- and the ferric center in truncated bacterial hemoglobins,[9] while a hydrogen-bond acceptor destabilizes the ferric state in Hemoglobin I from the clam *Lucina pectinata*, probably by deprotonation of the heme-bound H_2S.[10]

This interplay between an iron center, hydrogen sulfide, and hydrogen-bonding interactions prompted us to synthesize and characterize the first hydrogen(sulfido)iron complex, in which the sulfur-based ligand is stabilized by a hydrogen bond. The synthesis of mononuclear (hydrogen)sulfido complexes is challenging because the metal–SH fragments have a high propensity to form multinuclear species,[11] in particular with iron.[6e] This difficulty is highlighted by the small number of crystallographic structures of mononuclear (hydrogen)sulfido iron derivatives available in the literature.[12] It has to be noticed that all of these complexes are at the iron(II) state because of the strong reducing ability of hydrosulfide and that two of them were obtained with an indirect source of HS^-.[12b,d] Our strategy was to use a hexadentate ligand, previously described by Banse et al., that contains an oxygen-bonded carboxamidato moiety.[13] We anticipated that deprotonation of hydrogen sulfide by this basic fragment and subsequent coordination of the generated hydrosulfide anion would provide mild access to our targeted system (Scheme 1). As a support, in recent years, related

Scheme 1



approaches have been used to synthesize monomeric or dimeric iron(II) hydroxo complexes stabilized by intramolecular hydrogen bonds by deprotonation of water with deprotonated urea,[14] a pendant tertiary amine group,[15] or a deprotonated carboxamidato moiety.[16]

Complex $[(L)Fe]\cdot BPh_4$ (**1**), in which in addition to five nitrogen donors the iron(II) center is coordinated to the oxygen of a carboxamidato group, reacts with hydrogen sulfide in dichloromethane or acetonitrile to give the new derivative **2**.

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As is evidenced by monitoring the reaction by UV−vis spectroscopy (Figure 1), excess hydrogen sulfide is required

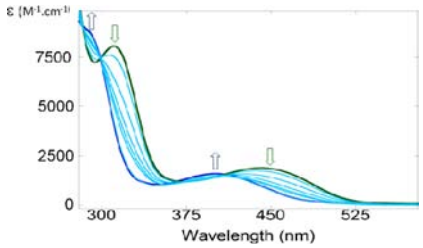

Figure 1. Evolution of the UV−visible spectrum of complex **1** (green, 0.07 mM in dichloromethane) upon the addition of 1, 2, 3, 4, 5, and 10 equiv of H_2S.

to ensure completeness of the reaction. The two absorptions corresponding to **1** are blue-shifted upon the addition of hydrogen sulfide, and the presence of four isosbestic points at 280, 297, 365, and 407 nm is indicative of a direct conversion of **1** to **2**. The electronic transition at lower energy (λ = 402 nm) is attributed to metal-to-ligand charge transfer by analogy with structurally related derivatives[13,17] and is typical of high-spin systems ($\varepsilon \approx 1500\ M^{-1}\ cm^{-1}$), which agrees with the effective magnetic moment in solution calculated by Evans method (μ_{eff} = 5.0 μ_B). Its significant blue shift compared to **2** is, however, less important than that observed on going from **1** to its protonated analogue $[(LH)Fe]\cdot 2BPh_4$ (**3**; λ = 383 nm), reflecting the relative strengths of the neutral carboxamidato, anionic hydrosulfido, and anionic carboxamido ligands. The second transition, at λ = 287 nm, is typical of a ligand-based $\pi-\pi^*$ transition. It is located at the same wavelength as that in **3**,[13] hinting that the carboxamidato moiety indeed acts as a base in this reaction. Further confirmation comes from the presence of a strong IR absorption at 1696 cm^{-1} (see Figure S2 in the Supporting Information), corresponding to the protonated amide carbonyl, as well as the presence of an exchangeable proton in ^1H NMR at −69.2 ppm, attributed to the N−H moiety.[18] However, no evidence for coordination of the hydrosulfide to the iron center is detected by these two spectroscopies.

The use of the intramolecular base is critical to cleanly preparing **2**: indeed, although the formation of **2** was detected during the reaction between complex **3** and 1 equiv of tetrabutylammonium hydrosulfide, it was always contaminated by a large amount of a black insoluble material (Figure S3 in the Supporting Information). To fully assess the structure of **2**, crystals were grown from a solution of **2** in dichloromethane layered with benzene. An ORTEP view of the structure of complex **2**, which cocrystallized with a solvent molecule, is presented in Figure 2.

The iron(II) center is in a pseudooctahedral environment, with the six positions being occupied by five nitrogen atoms from the amine/pyridine donor set and one sulfur atom from the (hydrogen)sulfido group. The coordination of HS^- and the release of the carboxamide function from the coordination sphere induce a rearrangement of the ligand backbone around the metallic center compared to the structure of **1**,[13] with Fe−$N_{pyridine}$ (average: 2.227 Å) and Fe−N_{amine} (average: 2.226 Å) bond distances typical of high-spin systems, in which they are expected to be close to 2.2 Å.[17a] The Fe−SH distance (2.387 Å) compares well with those recently reported for (hydrogen)-sulfido heme derivatives,[12e] and protonation of the carbox-

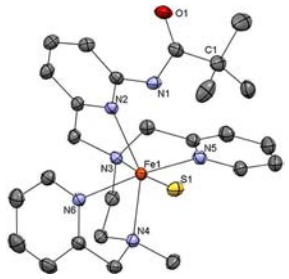

Figure 2. ORTEP view of complex **2** showing thermal ellipsoids at 50% probability and atom labeling. Hydrogen atoms, the CH_2Cl_2 molecule, and the BPh_4 anion are omitted for clarity. Selected bonds lengths (Å) and angles (deg) for **2**: Fe1−S1 2.387, Fe1−N_{py}(average) 2.227, Fe1−N_{amine}(average) 2.226, C1−N1 1.374, C1−O1 1.217; S1−Fe1−N3 173.73, N5−Fe1−N6 170.67, N4−Fe1−N2 144.78.

amidato moiety is clearly indicated by a shortening (1.217 vs 1.289 Å in **2** and **1**, respectively) of the C−O bond and an elongation of the C−N bond (1.374 vs 1.303 Å in **2** and **1**, respectively). The most interesting feature of the crystal structure is obviously the short N1−S1 bond (3.333 Å), which when correlated with the N−H···S angle (166.2°) clearly indicates a moderate hydrogen-bonding interaction[19] between the sulfur atom and the amide proton. Although the structure of a ferrous hydrogen(sulfido) complex based on a porphyrin with carboxamide pickets has been described,[12d] no hydrogen bonds were detected, with N−S bond lengths greater than 4.7 Å. In fact, there is so far in the literature only a single example of a hydrogen-bonded hydrogen(sulfido) metal complex, obtained fortuitously by the insertion of tolylisothiocyanate into a S−H bond of the complex $Cp^*Ir(PMe_3)(SH)_2$.[20]

The equilibrium (1) presented in Scheme 1 implies that complex **2** should behave as a hydrogen sulfide donor. Only few inorganic complexes are known to release hydrogen sulfide,[21] a feature that could be useful owing to the growing interest in biology for H_2S donors.[22] Among these, ruthenium complexes[21a,b,d] have been shown to reversibly coordinate H_2S or the dimeric rhodium complex $[\{Rh(\mu\text{-}SH)(CO)(PR_3)\}_2]$ to slowly equilibrate to give H_2S and the trinuclear complex $[Rh_3(\mu\text{-}H)(\mu_3\text{-}S)_2CO(PR_3)_3]$,[23] although both reactions must be carried out under anaerobic conditions. In this context, reversible protonation/deprotonation of the carboxamidato moiety between **1** and **2** could therefore provide a new strategy to release H_2S from a metallic center.

Indeed, solutions of analytically pure complex **2** in dichloromethane or acetonitrile are composed of a mixture of complexes **1** and **2** (35% and 65%, respectively, in a 5 mM solution in CD_3CN at 300 K) and hydrogen sulfide, under equilibrium.

Complex **2** is unreactive in solution toward dioxygen because its iron coordination sphere is saturated and the intramolecular hydrogen bond strongly reduces the electron density at the sulfur center. It is inert toward the addition of water up to 10 equiv in acetonitrile, with further addition leading to precipitation of the complex. Although the composition of the solution remains unchanged over 1 h, the slow evaporation of hydrogen sulfide gas progressively shifts the equilibrium (1) to the left, resulting in the almost complete back-conversion of **2** into **1** within 12 h, as shown in Figure 3.

On the other hand, if a hydrogen sulfide acceptor like the zinc complex $TpZnOH$[24] is added to a solution of **2**, **1** is instantaneously recovered, along with the formation of

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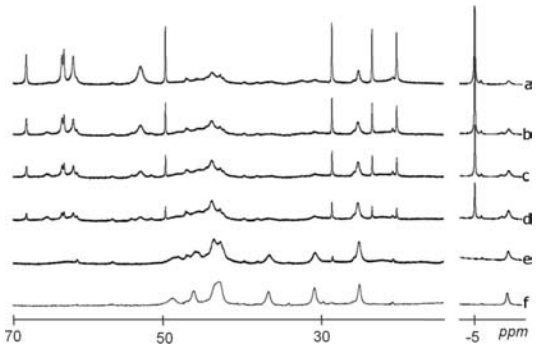
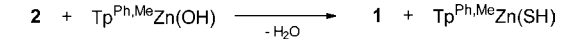


Figure 3. Zoom regions of the ^{1}H NMR spectra of complex **2** (5 mM in CD_3CN at 300 K) recorded at t = 0 (a) and then every 3 h (b−e) and the spectrum of **1** as a reference (f).

$TpZnSH$[25] (Scheme 2 and Figure S4 in the Supporting Information).

Scheme 2



CONCLUSION

Starting from an iron(II) complex with an oxygen-bonded carboxamidato group, which can be used as a base toward an exogenous acid ligand, we synthesized a rare example of a hydrogen(sulfido) complex stabilized by an intramolecular hydrogen bond. The reversibility of the reaction makes this FeSH complex a slow hydrogen sulfide donor in solution.

ASSOCIATED CONTENT

Supporting Information

Synthetic procedures and spectroscopic characterizations of complex **2** and crystallographic data for complex **2** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(18) The attribution is based on the apparition of the same signal when H_2S is replaced by PhSH to give $[(LH)Fe(SPh)]\cdot BPh_4$ (Figure S5 in the Supporting Information). The exchange most certainly takes place through the equilibrium (1) by reaction of **1** with D_2S.

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