How Do Oxidized Thioli Ligands Affect the Electronic and Reactivity Properties of a Nitrile Hydratase Model Compound?

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Nitrile hydratases (NHase) are non-heme Fe(III)-containing, or noncorrinoid Co(III)-containing, microbial enzymes that catalyze nitrile hydration. The iron form has been studied most extensively. The Fe(III) active site is low spin (S = 1/2), and ligated by three cysteines, two peptide amide nitrogens and either a sulfurs appear to be oxidized, one to a sulfenate (114 S cys (11); S(2)}

unstable, 7 and metal

properties of Fe-NHase can be nicely reproduced by six-coordinate

unmodified. To understand how the sulfinate and, possibly, the sulfenate sulfur influences the electronic and reactivity properties of NHase, we have synthesized a series of sulfur-ligated, five-coordinate Co(III) model complexes containing progressively more oxidized sulfurs.

Five-coordinate [Co(III)(S(2)Me(2)N(S(Pr)Pr))] (1) (Figure 1)16 is shorter than most Co(III) thiolates (average = 2.24 Å17–19 Azide and SCN bind quantitatively to 1 at room temperature to one of the thiolate sulfurs.20

Trigonal bipyramidal 1 (r = 0.87)21 is converted to a more square pyramidal (r = 0.48) sulfinate-thiolate-ligated complex, [Co(III)(S(2)Me(2)N(S(2)O)2N(S(Pr)Pr))] (1) (Figure 2),22 upon stirring in air for 3 days. Only one of the two thiolate sulfurs (S(2)) is oxidized, even upon prolonged stirring. Oxidation of S(2) causes the spin-state to change, from S = 1 (in 1) to 0 (in 2), and the reduction potential to shift cathodically to E1/2 = −380 mV vs SCE. The mean S(2)=O(1/2) distance (1.453(2) Å) in 2 falls in the usual range (1.42–1.48 Å).17,23,24 The Co–S(2) distance in 2 is indistinguishable from Co–S(1) (Figure 2). Both of the Co–S bonds in 2 are slightly shorter than the Co–S bonds in 1, because

Figure 1. ORTEP plot of [Co(III)(S(2)Me(2)N(S(Pr)Pr))] (1) showing 50% probability ellipsoids and the atom labeling scheme. H atoms have been omitted for clarity. Selected distances (Å) and angles (deg): Co–S(1), 2.162(2); Co–S(2), 2.158(2); Co–N(1), 1.923(4); Co–N(2), 2.060(5); Co–N(3), 1.923(4); S(1)–Co–S(2), 126.80(7); S(1)–Co–N(2), 117.3(1); S(2)–Co–N(2), 115.8(1).

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Addition of H$_2$O$_2$ to 2 results in the oxidation of the remaining thiolate to a sulfenate, and coordination of the added oxygen to the open coordination site. This reflects the stronger trans influence of sulfinate vs thiolate. Addition of H$_2$O$_2$ to 2 results in the oxidation of the remaining thiolate to a sulfenate, and coordination of the added oxygen to the open binding site, to form the thiolate to a sulfenate, and coordination of the added oxygen to the open coordination site. This reflects the stronger trans influence of sulfinate vs thiolate.


![Figure 2. ORTEP plot of [Co(III)(S$_{2}$SO$_{2}$)]$^{+}$ (2) showing 50% probability ellipsoids and the atom labeling scheme. All H atoms, except for the N–H proton, have been omitted for clarity. Only one of the two molecules contained in the asymmetric unit is shown. The second molecule is in a slightly different conformation ($\tau$ = 0.86). Selected distances (Å) and angles (deg): Co–S(1), 1.212(1); Co–S(2), 2.116(1); Co–N(1), 1.938(3); Co–N(2), 2.026(3); S(2)–O(1), 1.451(3); S(2)–O(2), 1.455(3); S(1)–Co–S(2), 110.9(1); S(1)–Co–N(3), 145.7(1); N(1)–Co–N(2), 174.8(2).](Image 105x621 to 244x744)

![Figure 3. ORTEP plot of [Co(III)((\eta$^2$-SO)(SO$_{2}$)]$^{+}$ (3) showing 50% probability ellipsoids and the atom labeling scheme. All H atoms, except for the N–H proton, have been omitted for clarity. Selected distances (Å) and angles (deg): Co–S(1), 2.132(1); Co–S(2), 2.118(1); Co–O(1), 2.042(2); Co–N(1), 1.957(3); Co–N(2), 1.943(3); Co–N(3), 1.993(3); S(1)–O(1), 1.548(3); S(2)–O(2), 1.454(3); S(2)–O(3), 1.464(3); S(1)–Co–S(2), 114.38(5); S(1)–Co–O(1), 43.5(1); S(1)–O(1)–Co, 71.4(1); S(1)–Co–N(3), 143.2(1); N(1)–Co–N(2), 173.6(1).](Image 368x621 to 507x744)


The Co(III) ion of 2 is in a lower spin-state. The observed spin-state change is caused by the geometry change. The geometric change is most likely driven by the sulfinate ligand’s preference for an apical site that lacks other ligands competing for overlap with the same p$_z$ orbital. In contrast to bis-thiolate ligated 1, sulfinate-ligated 2 does not bind N$_3^-$ or SCN$^-$ to its open coordination site. This reflects the stronger trans influence of sulfinate vs thiolate.

This work examines the influence that incremental oxidation of coordinated sulfur has on the reactivity and electronic properties of sulfur-ligated Co-NHase model compounds, and describes the first example of a model containing a sulfenate. The $\eta^2$-binding mode appears to prevent further oxidation of the sulfenate. The orientation of the sulfenate oxygen, syn to the open site, in the model described herein is identical to its orientation at the NHase active site. In our model, however, this orientation results in the coordination of the oxygen, and this shuts down reactivity. The work reported herein therefore suggests that if the sulfenate CoS$_{114}^{13-}$O were present in the active form of NHase, it might interfere with reactivity, and therefore its function, by blocking the reactive site. It is also possible that the protein prevents $\eta^1$-coordination of CoS$_{114}^{13-}$O, by providing H-bonds (from several arg residues contained in the active site pocket) that stabilize the deprotonated form. This study also shows that the strong trans influence of a sulfinate will cause (1) the geometry to change so as to place the open site opposite the sulfinate, (2) the spin-state to change, (3) the Co(II) oxidation state to become more accessible, and (4) reactivity to decrease at the open site.

2 -SO)(SO$_{2}$)]$^{+}$ (3) showing 50% probability ellipsoids and the atom labeling scheme. All H atoms, except for the N–H proton, have been omitted for clarity. Selected distances (Å) and angles (deg): Co–S(1), 2.132(1); Co–S(2), 2.118(1); Co–O(1), 2.042(2); Co–N(1), 1.957(3); Co–N(2), 1.943(3); Co–N(3), 1.993(3); S(1)–O(1), 1.548(3); S(2)–O(2), 1.454(3); S(2)–O(3), 1.464(3); S(1)–Co–S(2), 114.38(5); S(1)–Co–O(1), 43.5(1); S(1)–O(1)–Co, 71.4(1); S(1)–Co–N(3), 143.2(1); N(1)–Co–N(2), 173.6(1).