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Selective Oxidations of a Dithiolate Complex Produce a Mixed Sulfonate/Thiolate Complex

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Oxygenation or peroxidation of a planar, tetracoordinate, low-spin nickel(II) complex of a N_2S_2-donor ligand, (*N*,*N*′-dimethyl-*N*,*N*′-bis-(2-mecaptoethyl)-1, 3-propanediaminato)nickel(II), proceeds via the formation of a mixed sulfinate/thiolate complex and leads to the production of a novel dimeric complex containing both sulfonate and thiolate ligands. Thus, reaction proceeds via selective oxidation of the sulfinate sulfur atom, leaving the thiolate reduced. The novel sulfonate/thiolate complex has been isolated and characterized by electospray ionization mass spectrometry and single-crystal X-ray diffraction. Crystals form in the monoclinic space group $P2_1/c$ with cell dimensions $a = 8.4647(12)$ Å, $b = 12.592(3)$ Å, and $c = 12.531(2)$ Å, angles $\alpha = \gamma = 90°$ and $\beta = 106.645(11)°$, and $Z = 2$. The structure was refined to $R = 5.20\%$ and $R_w = 12.86\%$ [$I > 2\sigma(I)$]. The isolation of this mixed sulfonate/thiolate complex from oxidation of a mixed sulfinate/thiolate complex provides experimental evidence for the formation of a sulfonate ligand via a Ni–O–O–SO_2R intermediate, as suggested by recent density functional theory calculations.

The formation of cysteine *S*-oxygenates plays several important roles in biology.[1−3] These roles include tuning of the properties of metal cofactors featuring cysteine ligation.[4−7] In bacterial nitrile hydratases (NHases),[4−6] cysteine *S*-oxygenates are found bound to active site metals (Fe and Co) and exist in the presence of cysteine thiolate ligation. Crystallographic data[4] show that, in the iron-containing NHase from *Rhodococcus sp.* N-771, Cys_{112} and Cys_{114} are modified to sulfinic and sulfenic acids, respectively, while Cys_{109} remains reduced. Similarly, the crystal structure of a cobalt-containing NHase from *Pseudonacardia thermophila* shows that Cys_{111} and Cys_{113} are modified to the sulfinic and sulfenic acids, respectively, and coordinated[7] to cobalt(III) while Cys_{108} is unaltered. These structures raise the question of how three different oxidation states of sulfur form in the enzyme active sites. Here we report the first example of spontaneous oxidations of a dithiolate complex to form a complex containing one sulfonate and one thiolate ligand.

The neutral nickel(II) *cis*-dithiolate complex, (*N*,*N*′-dimethyl-*N*,*N*′-bis(2-mecaptoethyl)-1,3-propanediaminato)nickel(II) (**1**), was prepared according to published procedures.[8] The reaction of **1** with 3 equiv of H_2O_2 in dimethylformamide (DMF) yields the novel dimeric complex **2** (Scheme 1) in good yield (62%) following purification by silica gel column chromatography.[9] Crystals of the orange product suitable for single-crystal X-ray diffraction studies were obtained from a methanol solution upon the addition of ether.[10] The same product may be obtained by the reaction of the previously characterized mixed sulfinate/thiolate complex, **3**, with 1

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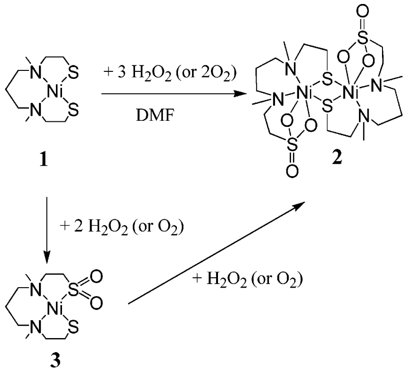
(9) Complex **1** (260 mg, 0.932 mmol) was dissolved in 50 mL of DMF at room temperature. To this solution was added 301 μL (2.791 mmol) of H_2O_2. The solution changed from red to orange. The mixture was left to stir under argon for 40 min, at which time the solvent was removed under vacuum. The resulting orange-brown solid was redissolved in a minimum volume of methanol/ethanol (1:1) and loaded onto a silica gel (Aldrich grade 62, 60−200 mesh) column (1.5 × 18 in.) made with dry methanol under N_2. Three fractions eluted with methanol/ethanol (4:1). The solvent from the second fraction was removed by vacuum to give 189 mg (62% yield) of an orange solid, **2**. This orange solid was redissolved in a minimum volume of methanol, layered with diethyl ether, and left at room temperature. Over a period of 4 weeks, yellow-orange crystals, suitable for X-ray diffraction, were isolated. Anal. Calcd for $Ni_2C_{18}H_{40}N_4S_4O_6 \cdot 2MeOH$ (**2**): C, 33.44; H, 6.73; N, 7.80. Found: C, 33.02; H, 6.58; N, 7.59. The solid-state magnetic susceptibility [$\mu_{eff} = 2.87\ \mu_B$ ($n = 2$)] was measured at ambient temperature using a Johnson-Matthey balance. The complex is largely diamagnetic in solution by NMR. IR (cm^{-1}): ν(S═O) 1020vs, 1130m, 1260s. UV−vis [DMF, λ (nm) (ϵ ($M^{-1}\ cm^{-1}$))]: 270 (2610), 285sh (2430), 308 (2620), 440 (190); consistent with a planar four-coordinate complex in solution. ESI-MS(+) (relative intensity): *m/z* 327.0 (100) cluster [calcd for $M^+ = (NiC_9H_{21}N_2S_2O_3^+)$, 327.0]. There is no evidence of the dimer, M_2^+, in the mass spectrum.

10.1021/ic051982h CCC: $33.50

Scheme 1. Reactions of (*N*,*N*′-Dimethyl-*N*,*N*′-bis(2-mercaptoethyl)-1,3-propanediaminato)nickel(II), Leading to the Formation of a Dimeric Mixed Sulfonate/Thiolate Complex



equiv of H_2O_2 or by the reaction of **3** with O_2, as shown in Scheme 1.

The molecular structure of **2** is summarized in Figure 1. Complete structural information can be found in the Supporting Information. The molecular structure of **2** reveals a dimeric complex with six-coordinate, high-spin Ni^{II} centers ($\mu_{eff} = 2.87\mu_B$, solid state).[9] Each Ni^{II} ion is bound by a $N_2O_2S_2$ ligand donor atom set, where the O donors are derived from a bidentate sulfonate group and the S donors are thiolates that bridge between the two Ni^{2+} ions. The Ni−Ni distance is 3.501(4) Å. The angles around the Ni are considerably distorted from ideal octahedral geometry. The O1−Ni−O2 angle involving the bidentate sulfonate ligand [62.28(19)°] is particularly constrained and thus leads to considerable distortion of the other *trans*-ligand angles. The three S−O bonds are clearly not identical; the non-Ni-bonding S1−O3 distance is shorter than the liganding S1−O1 and S1−O2 bonds. This situation is similar to that found in other O-bound nickel sulfinates and sulfonates.[11−15] The differences in bond lengths also suggest a decrease in the double-bond character for the liganding S1−O1/O2 bonds. The dinuclear complex resides on a crystallographic inversion center, and the Ni−S−Ni angles [93.77(7)°] are close to 90°. The Ni_2S_2 rhomb is planar, a feature that is not uncommon in centrosymmetric S−S edge-sharing dinuclear six-coordinate Ni complexes.[8,12,16−18]

The IR spectrum of **2** has one strong absorption at 1020 cm^{-1} that can be assigned to $\nu(S{=}O)$ stretching vibrations. This frequency is around 100 cm^{-1} higher than the corresponding Ni−SO assignments reported for related nickel sulfur oxygenates.[19−21]

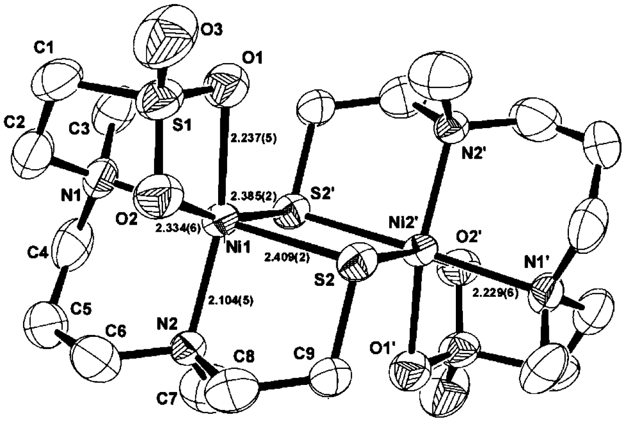


Figure 1. ORTEP plot of **2** with ellipsoids at 50% probability. Hydrogen atoms have been excluded for clarity. Numbers indicate first-coordination-sphere metal−ligand distances (standard deviation) in angstroms.

The electospray ionization mass spectrometry (ESI-MS) spectrum of complex **2** shows an intense isotopic cluster at $m/z = 327.0$, corresponding to the monomeric monosulfonate complex (see the Supporting Information). There is no indication of the dimeric species in the ESI-MS spectrum, suggesting either that it does not exist in solution or that the ESI-MS experimental conditions are harsh enough to cleave the dimer. The dithiolate complex **1** has previously been shown to produce a planar four-coordinate monosulfinate complex upon oxidation with O_2.[22] The formation of **2** was also detected during the oxygenation of the monosulfinate complex but was not isolated. The UV−vis spectrum of a sample taken during the oxygenation of the monosulfinate matches that of isolated **2**, and the ESI-MS spectrum of a sample taken during the oxygenation shows that after 11 h at 40 °C the most abundant species present is **2**, which gives rise to the isotopic cluster of peaks at $m/z = 327.0$ that are characteristic of the ESI-MS spectrum of **2** (Figure 2).

The preferential oxidation of either a dithiolate or a mixed sulfinate/thiolate complex to form a complex with mixed sulfonate/thiolate thiolate ligation has not been previously observed. Similar chemistry has been examined in detail for peroxidations of cobalt and chromium thiolates[23] as well as for a number of other planar four-coordinate nickel(II) dithiolate complexes.[8,11,19−22,24−32] These systems have in

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(10) Crystals of **2** form in the monoclinic space group $P2_1/c$ with cell dimensions $a = 8.4647(12)$ Å, $b = 12.592(3)$ Å, $c = 12.531(2)$ Å, $\alpha = \gamma = 90°$, $\beta = 106.645(11)°$, and $Z = 2$. The structure was refined to $R = 5.20\%$ and $R_w = 12.86\%$ [$I > 2\sigma(I)$]. See the Supporting Information for details.

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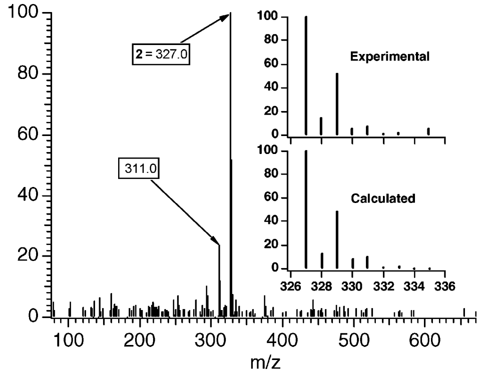
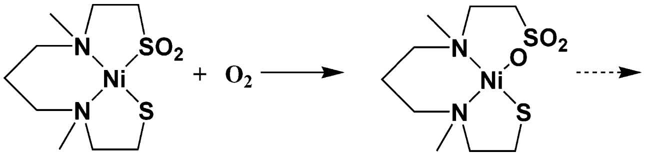


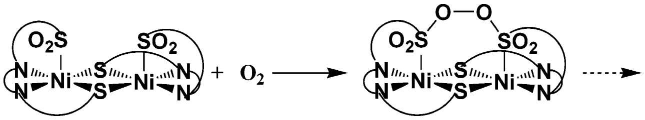
Figure 2. ESI-MS spectrum of a sample taken during the oxygenation of the monosulfinate of **1** at 40 °C in DMF ($t = 11$ h). The cluster at *m/z* 327.0 (100) corresponds to **2**. The cluster at *m/z* 311.0 (24) corresponds to **3**, $(NiC_9H_{21}N_2S_2O_2)^+$. Inset: expanded mass spectrum of the *m/z* 327.0 region and a spectrum calculated by assuming the formula for the monomer $(NiC_9H_{21}N_2S_2O_3{}^+)$ and monoisotopic masses employing the most abundant isotopes.

common the presence of a metal that does not easily undergo redox chemistry and thus favors S-centered redox. Further, each of these systems (Co^{III}, Cr^{III}, and low-spin Ni^{II}) typically exhibits sluggish ligand-exchange rates and thus may exhibit S-oxygenation instead of disulfide formation for these reasons. The nickel(II) dithiolate chemistry advances the understanding of reactivity and reaction mechanisms by affording systems where the relative reactivity of two thiolates may be addressed. Prior studies have yielded structurally characterized complexes featuring sulfenate/thiolate,[19−21,30] sulfinate/thiolate,[19,20,25,30−32] sulfinate/sulfenate,[21] disulfenate,[21,31] disulfinate,[19] and disulfonate[20,32] coordination derived from the peroxidation or oxygenation of nickel(II) *cis*-diaminodithiolates. These reactions suggested that oxidation of the first thiolate instead of the second one would be expected to stop at the sulfinate level until the second thiolate was also oxidized to a sulfinate. However, density functional theory calculations of possible intermediates in the oxygenation of a monosulfinate to the fully oxidized disulfonate product predicted that an $Ni-O-O-SO_2R$ species is a more favored intermediate than the disulfinate and would eventually lead to the disulfonate product by way of a monosulfonate/thiolate intermediate.[32] The isolation and characterization of **2** provides experimental evidence for the viability of this reaction pathway.

Scheme 2



Scheme 3



The monosulfonate, **2**, is a dimer that is formed by placing the remaining thiolates in bridging positions. At first glance, this might account for the formation of the monosulfonate because of the lower reactivity of bridging thiolates.[22,33] However, the starting material is monomeric in the solid state, and there is no evidence to support the formation of stable dimers in solution.[9] Further, the formation of a high-spin Ni^{II} complex, such as **2**, would be expected to exhibit rapid ligand-exchange kinetics, and the long (and presumably weak) $Ni-S_{bridge}$ bonds (2.4 Å) are unlikely to support stable dimer formation in solution. The oxidation of the monosulfinate derived from **1** by reaction with O_2 is very slow, but it still leads to the formation of **2**, and transient dimer formation would not be expected to provide protection from oxidation of the thiolates. Although it remains under current investigation, it appears more likely that **2** results from a peroxide-like (monoxygenase) transfer of one O atom from O_2, consistent with the prediction from theory (Scheme 1),[32] rather than from a dioxygenase-like reaction (incorporation of both O atoms from the same O_2 unit; Schemes 2 and 3) previously described for sulfinate formation with O_2.[8,25,31,32]

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Supporting Information Available: ESI-MS spectrum of **2**, tables of crystallographic data for **2**, and a CIF file. This material is available free of charge via the Internet at http://pubs.acs.org.

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