Template Effect for O_2 Addition across *cis*-Sulfur Sites in Nickel Dithiolates

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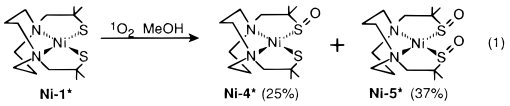
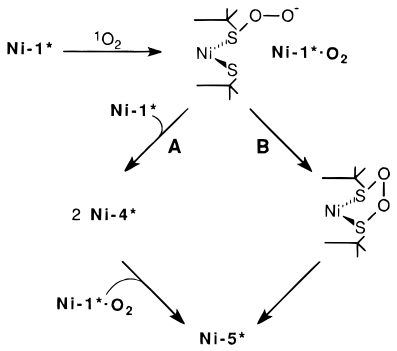
The reaction of O_2 with metal thiolates is known to inhibit activity and irreversibly deactivate sulfur-rich enzymes such as CO-dehydrogenase and [NiFe] hydrogenase.[1] Whereas typical products of thiolate oxidative degradation are di- or polysulfides, the *cis*-dithiolates [1,5-bis(2-mercaptoethyl)-1,5-diazacyclooctanato(2−)]nickel(II), **Ni-1**, and its sterically hindered analogue, **Ni-1***, are relatively rare examples of compounds which yield isolable and separable S-oxygenates, primarily $M(SO_2R)$, on reaction with O_2.[2−5] Since reaction of the diamagnetic **Ni-1*** with $^3O_2$ is spin forbidden, yields and rates can be greatly increased through the use of $^1O_2$. In methanol, the product distribution is as found in eq 1.[6] The appearance of **Ni-5*** raised the question of whether O_2 addition occurred via successive O-atom additions, as in the case of H_2O_2, or by molecular O_2 addition across adjacent S-sites.[3,7] This mechanistic problem has been addressed by analysis of **Ni-5*** produced from the photosensitized oxygenation of **Ni-1*** with a mixture of $^{16}O_2$/$^{18}O_2$ by positive electrospray ionization mass spectrometry.

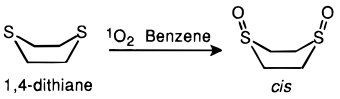


(1)

Similar queries have arisen in organosulfur chemistry. For example, the appearance of the *cis*-disulfenate exclusively as the product from the reaction of $^1O_2$ with the conformationally constrained 1,4-dithiane was taken as evidence of the feasibility of intramolecular O_2 addition across adjacent sulfur sites, eq 2.[8] However, this conclusion is questioned by the fact that oxygenation of the monosulfenate of 1,5-dithiacyclooctane yields solely the *cis* isomer of the disulfenate; i.e., intermolecular paths of oxygen atom transfer also yield the *cis* isomer exclusively.[9] To our knowledge, the defining mechanistic isotopic labeling experiment has not been reported in these systems. However, $^{18}O_2$/$^{16}O_2$ experiments have shown intramolecular addition of O_2 to disulfides to yield thiosulfonates.[10] Also, formation of sulfone was shown by isotopic labeling to occur via intramolecular O_2 addition to phenyl methyl sulfide but via intermolecular O_2 addition to diethyl sulfide.[10,11]

Scheme 1





(2)

The concept of adjacent sulfur site addition to *cis* sulfurs of transition metal complexes has precedence in the reactions of dimolybdenum complexes with olefins and dihydrogen.[12,13] The question of whether the O_2 is adding as a molecule across the adjacent sulfur sites of **Ni-1*** followed by *intramolecular* O−O scission or if *intermolecular* O−O scission is occurring with production of **Ni-5*** preceded by **Ni-4*** may be addressed by differentiating the two most likely mechanisms of bissulfenate formation given in Scheme 1. Path A represents intermolecular oxygen addition while path B shows intramolecular addition. Both paths derive from a persulfoxide type precursor as shown in Scheme 1. This precursor is based upon the proposed intermediate for the reaction of singlet oxygen with organic sulfides in protic solvents.[8]

In a typical experiment 34.7 mg (0.100 mmol) of **Ni-1*** and ca. 1 mg of rose Bengal, a $^1O_2$ sensitizer, were placed in a 50 mL Pyrex Schlenk tube and thoroughly degassed prior to addition of 6 mL of dry, degassed methanol.[14] A slight negative pressure was drawn on the solution, and the flask was backfilled with a $^{18}O_2$/$^{16}O_2$ mixture to a slightly positive pressure. The $^{18}O_2$:$^{16}O_2$ ratio was determined immediately before addition by GC/MS (HP5995C). The solution was irradiated via a medium pressure Hg vapor lamp for 2 × 30 min, following which the solvent was removed under vacuum. Separation on a silica gel column eluted with dry methanol yielded pure **Ni-5*** for mass spectral analysis.

Positive ion electrospray ionization (ESI) mass spectra were obtained on a Vestec 201 quadropole mass spectrometer (Vestec Corp., Houston, TX) having a mass range of 1200 amu. A heated ESI source was used as described previously.[15,16] Mass spectra were recorded on a Technivent Vector One (Technivent Corp, Maryland Heights, MO) data system interfaced with an IBM-compatible 80386 personal computer. ESI-MS was used

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(6) A 17 mM methanolic solution of **Ni-1*** was irradiated for 2 × 30 min in a Pyrex photochemical reactor as O_2 was slowly bubbled through solution. Approximately 1 mg of Rose Bengal was added as sensitizer. Separation of oxygenates was performed as described in ref 3.

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(14) Photolysis performed in the absence of sensitizer produced no oxygenated product eliminating the possibility that excitation of nickel is required. In addition, $^1O_2$ produced by thermal decomposition of 1,4-dimethylnaphthalene endoperoxide reacted with **Ni-1*** yielding the same products in the absence of light as the photochemically produced $^1O_2$.

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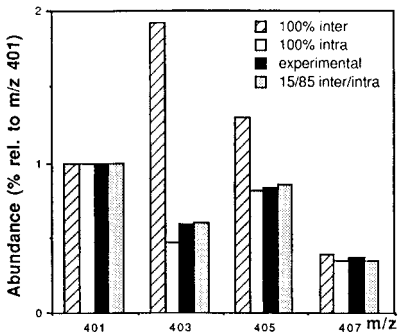


Figure 1. Theoretical and experimental ion abundances for the mass spectrum in the $[M + Na]^+$ of **Ni-5*** from the reaction of **Ni-1*** with a 58:42 mixture of $^{16}O_2/^{18}O_2$.

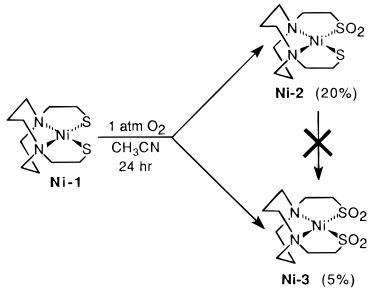
to determine relative isotopic abundances in the **Ni-5*** plus Na^+ (from the silica column) product ions. Each analysis generated a mass spectrum composed of the average of approximately 50 scans. Three analyses were performed per sample.

Figure 1 shows the experimental abundances of the [**Ni-5*** + Na]$^+$ ion in the *m*/*z* 401−407 region. Also shown in Figure 1 are the theoretical abundances for 100% intramolecular and 100% intermolecular addition determined using the natural isotopic abundances of Ni [^{58}Ni (68.27%), ^{60}Ni (26.10%), ^{62}Ni (3.59%)] and S [^{32}S (95.02%), ^{34}S (4.21%)] and the experimental isotopic abundance of O [^{16}O (58%), ^{18}O (42%)].[17] Although all of the isotopes listed above were used in the calculations, for simplicity only those with an abundance greater than 5% will be used for discussion. The abundances of *m*/*z* 401 and 403 ions have the greatest expected differences and will be used for comparison. Regardless of the pathway, *m*/*z* 401 is due to the single isotopomer $^{58}Ni^{16}O^{16}O$ and it was chosen as the standard. If intermolecular O_2 addition is occurring, the signal at 403 will arise from the combination of $^{58}Ni^{16}O^{18}O$ and $^{60}Ni^{16}O^{16}O$. Intramolecular addition would only produce a $^{60}Ni^{16}O^{16}O$ signal at 403. The bar graph of Figure 1 compares the theoretical abundances for *m*/*z* 401 and 403 for intermolecular (1:1.92) and intramolecular (1:0.47) addition, respectively. The experimental ratio is 1:0.60, clearly a better match for the latter. Instrument reproducibility and accuracy were checked by analysis of **Ni-5*** prepared from natural abundance O_2, which yielded results within 5% of the predicted values. Inclusion of a small amount (15%) of intermolecular addition increases the theoretical ratio for *m*/*z* 401:403 to 1:0.56. A repeat experiment using $^{16}O_2$ (77%) and $^{18}O_2$ (23%) with a predicted 401:403 ratio of 1:1.07 for path A and 1:0.47 for path B is shown in the bar graph in Figure S1 (supporting information). Again, the experimental ratio is 1:0.60. The theoretical ratio rises to 1:0.61 when 15% intermolecular addition is included. Although the data clearly shows that the majority of product is generated via intramolecular addition, as much as 15% (±5) of the product may be formed by intermolecular addition.[18]

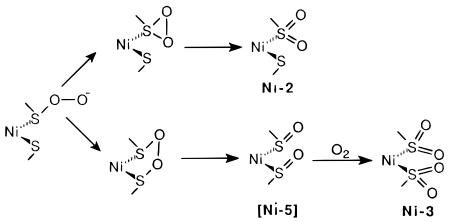
The results obtained also serve to substantiate a previous proposal of a dual-pathway oxygen addition mechanism. When exposed to $^3O_2$, **Ni-1** reacts to yield the sulfinato and bissulfinato complexes as shown in Scheme 2.[19]

The lack of further reactivity of isolated **Ni-2** is consistent with the deactivation of S-site nucleophilicity upon conversion of an adjacent thiolate S donor to a sulfinate donor, thus relieving the $Ni_{d-\pi}-S_{lonepair}$ 4-electron destabilization.[4,20] Isotopic labeling studies show that while **Ni-2** contains oxygens from the same O_2 molecule, SO_2 fragments from **Ni-3** contain oxygens from different O_2 molecules.[19,21] These results were

Scheme 2



Scheme 3



interpreted in terms of two independent pathways in which **Ni-3** has precursors including a nickel heterocycle and the bissulfenate **[Ni-5]**, Scheme 3. Although **Ni-5** has never been isolated, the sterically hindered **Ni-5*** provides corroboration of this two-path mechanism.

The ability to track the isotopomers of O_2 during S-oxygenation of **Ni-1** and **Ni-1*** presents a powerful case for adjacent site O_2 reactivity as well as for the reaction pathways which retain the M−S bond as the oxidation/oxygenation of sulfur ensues. The remarkable increase in reaction rate and yield for the oxygenation reaction of **Ni-1*** upon excitation of $^3O_2$ to $^1O_2$ also attests to S-based chemistry in the rigorously square planar **Ni-1***, which resembles the reactivity of organic sulfides with $^1O_2$. In fact, studies of photostabilization agents for polyolefins have found that $Ni(SR)_4^{2-}$ complexes quench $^1O_2$ with an efficiency comparable to that of the organic antioxidant β-carotene.[22] However, those studies only dealt with the rate of $^1O_2$ loss and did not explore the possibility of discrete S-oxygenates or O_2 uptake in the products. Our findings clearly prove that the latter is an important process in the $^1O_2$ quenching ability of Ni thiolates. Although $^3O_2$ reacts more slowly than $^1O_2$, with either the oxygen eventually resides on sulfur in the Ni thiolates and must be considered as a strong possibility in O-damaged catalytic sites. Particularly important is the fact that adjacent sulfur sites connected by a d^8 metal play a unique role in intramolecular addition and O−O bond scission.

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Supporting Information Available: Calculations of the theoretical *m*/*z* abundances for 100% intramolecular, 100% intermolecular, and 85%/15% intramolecular−intermolecular addition and Figure S1 displaying experimental and theoretical ion abundances for **Ni-5*** when $^{16}O_2/^{18}O_2$ equals 77%/23% (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(18) The presence of some products of the intermolecular addition path is not unexpected. In fact, the selectivity shown by **Ni-1*** is remarkable in view of the responsiveness of the sensitized photooxygenation reactions of organic sulfides to solvent, concentration, and temperature.

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