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Selective Sulfoxidation of Thioethers and Thioaryl Boranes with Nitrate, Promoted by a Molybdenum−Copper Catalytic System

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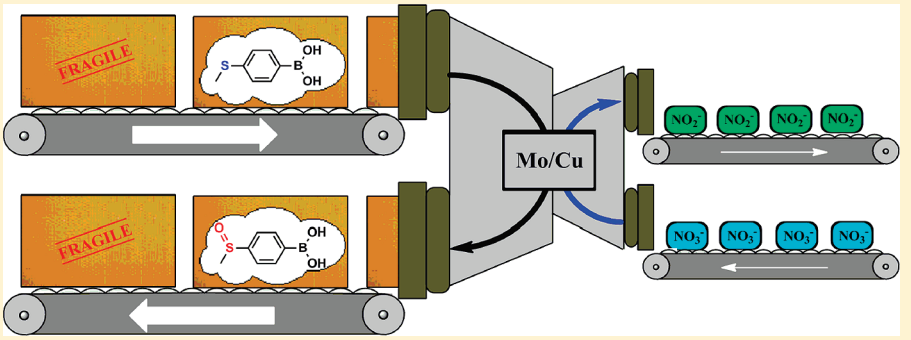
Supporting Information

ABSTRACT:



The catalytic reduction of nitrate by molybdo-enzymes plays a central role in the global biological cycle of nitrogen. However, the use of nitrates as oxidants in synthetic organic chemistry is very limited and typically requires very strong acidic and other extreme reaction conditions. We have developed a highly chemoselective and efficient catalytic process for the sulfoxidation of thioethers and arylthioethers containing boronic acid or boronic ester functional groups, using nitrate salts as oxidants. This homogeneous catalytic reaction was carried out in acetonitrile, where the $MoO_2Cl_2(OPPh_3)_2$ complex **1** or a mixture of complex **1** with $Cu(NO_3)_2$ were used as catalysts. We examined the reaction mechanism using ^1H, ^{15}N, and ^{31}P NMR techniques and ^{18}O-labeled sodium nitrate ($NaN^{18}O_3$) and show that the thioethers are oxidized by nitrate, generating nitrite. Our work adds to the existing chemical transformations available for organoboron compounds, providing straightforward accessibility to a variety of new substrates that could be suitable for Suzuki cross-coupling chemistry.

1. INTRODUCTION

Oxygen-atom-transfer (OAT) reactions promoted by complexes containing $[MoO_2]^{2+}$ cores are a topic of significant interest in the fields of chemistry and biology, partly because of their integral role in the global biological cycle of nitrogen[1] and their presence in many important metalloenzymes, such as cytochrome P450, sulfite oxidase, DMSO reductase, and nitrate reductase.[2] The denitrification pathway, responsible for the reduction of nitrate, is an excellent example of inorganic biochemistry at work.

Over the past 30 years, dioxomolybdenum complexes have been prepared and characterized as possible structural analogues of the active site of nitrate reductase.[3] Typically, biomimetic systems promote OAT processes by catalytic reduction of a variety of substrates with tertiary phosphines.[4] Although tertiary phosphines are not physiological substrates, they became the reagents of choice for studying OAT reactions and their mechanisms, both because of tertiary phosphines' high solubility in organic solvents and because of the fact that their reactivity can be fine-tuned through substitution of functional groups on the phosphorus atom. However, with a motivation to expand the scope of this reaction, we intended to test whether molybdenum-based catalytic systems can promote oxidation of thioethers, instead of more reactive tertiary phosphines, using very mild oxidants.

Previous studies have demonstrated the oxidation of thioethers into corresponding sulfoxides, with satisfactory chemoselectivity, by HNO_3 with the use of oxygen, catalyzed by gold halides.[5] In addition, researchers demonstrated catalytic systems that use a combination of $BiBr_3$ and $Bi(NO_3)_3$ in HNO_3 (with addition of NaBr or KBr), supported on silica gel or polyvinylpyrrolidone.[6] It should be mentioned that for many substrates the use of fuming nitric acid may lead to a formation of substantial amounts of undesired side products.

Selective sulfoxidation of thioethers has a broad range of applications, and since many sulfoxides exhibit a significant bioactivity, such a transformation was proved to be very useful in the development of compounds for pharmaceutical and agrochemical industries.[7]

Oxidation of thioethers with the use of Lewis-acid catalysts is an important reaction in organic synthesis, where H_2O_2 is

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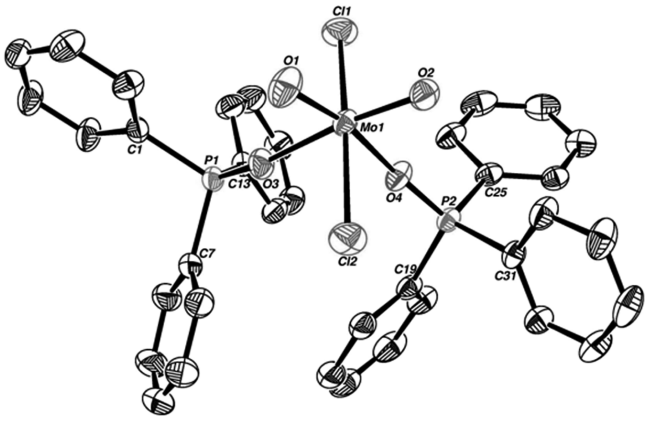

Figure 1. X-ray crystal structure of $Mo^{VI}O_2Cl_2(OPPh_3)_2$ complex **1**.

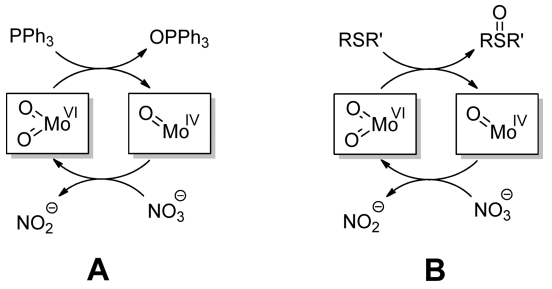

Figure 2. (A) Catalytic reduction of nitrate salt with tertiary phosphine. (B) Catalytic reduction of nitrate salts with thioethers via the OAT process; both promoted by complex **1**.

frequently used as an oxidant.[8] However, the methods that are currently reported rarely provide the ideal combination of selectivity, fast reaction kinetics, and high product yields.[9] Also, the presence of boronic functional groups in a thioether substrate can be problematic due to a simultaneous oxidation of the boronic group.[10] Thus, the chemoselective sulfoxidation of thioethers, containing boronic acid or boronic esters, is a challenging task.

To the best of our knowledge, using nitrate salts for the sulfoxidation of thioethers, catalyzed by dioxomolybdenum complexes, is unprecedented. The well-known dioxomolybdenum complex $Mo^{VI}O_2Cl_2(OPPh_3)_2$ (**1**) (Figure 1) is a member of the $Mo^{VI}O_2X_2L_2$ (X = Cl, Br, F; L = OPR_3) compounds family, which is known as catalysts for the selective epoxidation of olefins with *tert*-butyl-hydroperoxide.[11] The IR spectra and X-ray structures of these complexes have been reported, and their mechanism of the catalytic olefin epoxidation has been investigated in detail by several groups.[12] However, no catalytic activity, involving nitrate reduction with concomitant oxidation of tertiary phosphines, has been reported for this family of molybdenum compounds, until now.

Our work was focused on oxidation of thioether substrates, instead of tertiary phosphines, where nitrate salts were used in these reactions as the oxygen source. To the best of our knowledge, this is the first demonstration of a mild and high-yield method for the selective sulfoxidation of thioethers, with nitrate salts, promoted by molybdenum-based catalytic systems. The method offers the advantage of compatibility with a wide range of functional groups, with no overoxidation of thioethers to corresponding sulfones. Our catalytic system provides also the first example of high-yield selective sulfoxidation of arylthioethers containing boronic acid or boronic ester functional groups. We studied a mechanism of this OAT reaction and evaluated the catalytic activity of complex **1**-based systems by multinuclear NMR and mass spectrometry methods and by using isotope-labeled nitrate salts.

2. RESULTS AND DISCUSSION

A common preparation route for the complex **1** relies on treatment of molybdic acid in aqueous HCl with PPh_3.[13] We developed a new synthetic procedure, which included reaction of $Mo^{VI}O_2Cl_2$ with H_2O_2 in CH_3CN. Subsequent addition of PPh_3 produced the complex **1** in a quantitative yield. Recrystallization of the complex **1** from CH_3CN at room temperature gave crystals suitable for a single-crystal diffraction. The complex **1** structure was characterized by X-ray crystallography, revealing a distorted octahedron, with approximately C_{2v} symmetry. The results of X-ray photoelectron spectroscopy indicated that complex **1** has an oxidation state similar to a reference $Mo^{VI}O_2Cl_2$ compound, and the structure of **1** was found to be similar to that of the published data.[14]

In the preliminary experiments, we used complex **1** as the catalyst to test its activity in the reduction of the nitrate salts to the corresponding nitrites, in the OAT reaction with PPh_3. The reaction was carried out in CH_3CN at room temperature, and the results showed complete conversion of PPh_3 to triphenylphosphine oxide ($OPPh_3$) and of nitrate to nitrite (Figure 2A).

Upon successful reduction of nitrate to nitrite with PPh_3, promoted with complex **1**, we performed a series of sulfoxidation reactions with various thioethers and tetrabutylammonium nitrate (TBAN), as the oxidant. These reactions were conducted in the presence of catalytic amounts of complex **1**, with and without addition of catalytic amounts of $Cu(NO_3)_2$. The kinetics of the sulfoxidation reactions of substrates 1−14 (Table 1) were measured initially when the systems were exposed to air and then under argon. No significant changes in yields were found in both cases, and the reactions proceeded to completion independently of the reactions' atmosphere. Optimization of the reaction conditions (e.g., solvent and temperature) revealed that highly efficient sulfoxidations took place in CH_3CN at 60 °C. Under these conditions, most of the examined reactions proceeded well, with low catalyst loading (2 mol %), and a typical turnover number of 50 was achieved after 10 h. The substrates and products of these reactions are listed in Table 1.

Control experiments showed that in the absence of the complex **1** no reaction took place between nitrate salts and thioethers (1:1 molar ratio at 60 °C for 10 h). We found that substrates with electron-withdrawing groups, such as 4-bromothioanisole, phenoxathiin, and phenyltrifluoromethyl thioether (entries 3, 5, and 10, Table 1) gave relatively low yields of products. In these and other cases, an addition of catalytic amounts of $Cu(NO_3)_2$ to the reaction mixtures had a dramatic effect on the reaction outcome, as reflected by obtained higher yields, in comparison to reactions catalyzed only by the complex **1**. For the dialkylthioether substrates (entries 8 and 9, Table 1), the resulting oxidation yields to the corresponding sulfoxides were also improved upon addition of $Cu(NO_3)_2$. In contrast, in the cases of 4-methoxythioanisole (4MTA; entry 1, Table 1), containing a strong electron-donating group, and of 2-(methylthio)naphthalene (entry 4, Table 1), addition of $Cu(NO_3)_2$ had no effect on the overall yields nor on the reaction rates.

Notably, a selective sulfoxidation of thioarylborane acids and esters (entries 11−14, Table 1), compounds containing two different oxidizable groups, occurred in our OAT reactions without

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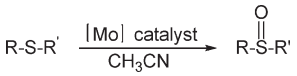
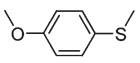
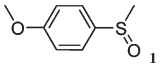
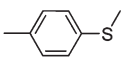
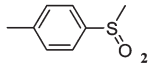
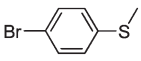
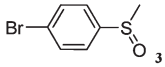
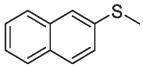
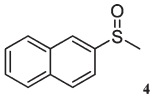
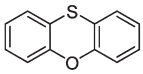
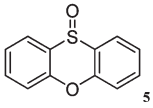
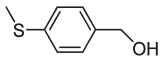
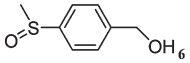
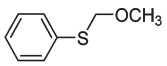
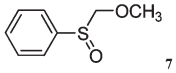
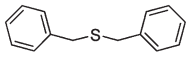
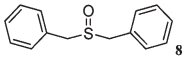
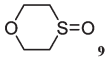
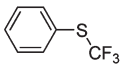
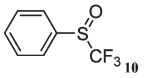
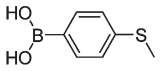
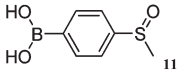
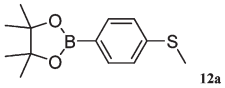
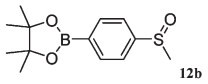
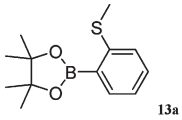
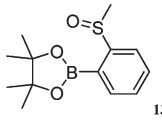
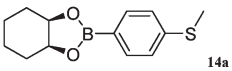
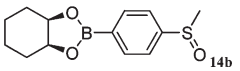
Table 1. Oxidation Reactions of Various Thioethers Promoted by Complex 1, With and Without the Presence of a Catalytic Amount of $Cu(NO_3)_2$[a]



Entry	Thioether	Product	Yield complex 1 [%][a]	Yield complex 1 with addition of $Cu(NO_3)_2$ [%][b]
1		 1	> 99	> 99
2		 2	76	> 99
3		 3	15	75
4		 4	35	40
5		 5	<1	> 99
6		 6	> 99	> 99
7		 7	75	> 99
8		 8	5	75
9		 9	20	35
10		 10	30	70
11		 11	35	> 99
12	 12a	 12b	30	> 99
13	 13a	 13b	35	> 99
14	 14a	 14b	25	45

[a] Reaction conditions: [a] thioether (1.25 mmol), TBAN (1.25 mmol), complex **1** (0.025 mmol), 60°C, 10 h; [b] thioether (1.25 mmol), TBAN (1.25 mmol), complex **1** (0.025 mmol), $Cu(NO_3)_2$ (0.025 mmol), 60°C, 10 h.

any changes in the boronic groups. The yields of these reactions were markedly improved from about 30% to the quantitative (entries 11−13, Table 1), when complex **1** was used in combination with $Cu(NO_3)_2$.

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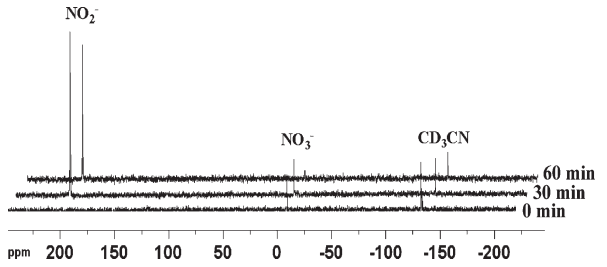


Figure 3. Stacked plot of ^{15}N NMR spectra in monitoring of the 4MTA sulfoxidation with complex **1** as a catalyst and $Na^{15}NO_3$ as the oxidant.

Monitoring the reaction progress by ^{15}N NMR, the appearance of the nitrite and disappearance of nitrate ions were evident, in a catalytic reaction with complex **1**, as can be seen in the stacked-plot spectra shown in Figure 3. The use of a ^{15}N-labeled nitrate in 4MTA sulfoxidation experiments, promoted by complex **1** or by a mixture of complex **1** and $Cu(NO_3)_2$, clearly exhibited the decay of a nitrate ion peak at 0 ppm and the buildup of a nitrite ion signal at 200 ppm. The formation of nitrite was also confirmed by Griess's reagent, while control experiments were conducted to validate that no false positive responses are observed in the absence of the catalyst in the reaction mixtures. This study indicated that the nitrate is converted directly to nitrite in our OAT process.

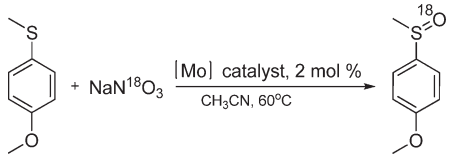
The next step in our study of the reaction mechanism was to monitor the OAT from the nitrate oxidant to the thioether substrate. For this purpose, we used ^{18}O-labeled sodium nitrate ($NaN^{18}O_3$), for oxidation of 4MTA (Scheme 1). The reaction products, detected by high-resolution chemical-ionization mass spectrometry, revealed a mixture of ^{18}O- and ^{16}O-labeled sulfoxides. The process of oxygen exchange between water and ^{18}O-labeled nitrate, at elevated temperatures under acidic conditions, has already been described in the literature for preparation of ^{18}O-enriched nitrate.[15] Our findings showed that the latter process leads to a partial isotope dilution of the enriched nitrate ions, resulting in somewhat lower-than-expected amounts of ^{18}O-labeled sulfoxide products. Control experiments showed that attempts to oxidize, without or with a catalytic amount of nitrate ions, and in the presence of air, as potential oxidant,[16] failed to give the sulfoxide product. Therefore, the presence of ^{18}O-labeled 1-methoxy-4-(methylsulfinyl)benzene (oxidized 4MTA) in the reaction mixture clearly shows that nitrate is the source for the oxygen atom in our sulfoxidation reactions promoted by complex **1** or by a mixture of complex **1** with the $Cu(NO_3)_2$ catalytic system.

All attempts to resubject the 1-methoxy-4-(methylsulfinyl)-benzene to further oxidation to the corresponding sulfone derivative under developed OAT conditions were unsuccessful, showing again a high selectivity of our process.

The sulfoxidation reaction was also studied by ^{31}P NMR spectroscopy. The spectrum of complex **1** showed only one signal at 40 ppm, which was assigned to the molybdenum-coordinated $OPPh_3$ (free $OPPh_3$ was found to exhibit a chemical shift of 30 ppm in CD_3CN). The single peak in complex **1** indicates that both phosphorus atoms in this complex are equivalent.

The reaction of 4MTA with TBAN (in 1:1 molar ratio), promoted by complex **1**, was monitored by ^{31}P and ^{1}H NMR. Over time, the peak intensity of the molybdenum-bound $OPPh_3$ decreased with the concomitant increase in the peak intensity of a dissociated free $OPPh_3$, indicating reversible binding of the $OPPh_3$ ligand. The sulfoxides, generated in the reaction mixture,

Scheme 1. ^{18}O-Transfer Experiment with 4MTA



proved to be a better ligand than $OPPh_3$, successfully competing for the coordination to the molybdenum metal center. These results may explain the dissociation of the $OPPh_3$ during the reaction.

The ^{31}P NMR spectrum of a mixture containing complex **1** and an equivalent amount of $Cu(NO_3)_2$ exhibited two single peaks of the same intensity and integration (at 44 and 54 ppm), indicating that coordinated $OPPh_3$ ligands lost their equivalence in the complex. Measurements of this mixture on NMR spectrometers with different magnetic fields (81, 162, and 202 MHz) showed that the observed chemical shifts were independent of the field, as opposed to splitting constants.

Upon monitoring the OAT process between 4MTA and TBAN (1:1 molar ratio), catalyzed by a mixture of complex **1** and $Cu(NO_3)_2$, we observed a gradual and simultaneous disappearance of both phosphorus peaks with the same rate, which clearly indicates the formation of paramagnetic active homogeneous catalyst (see Supporting Information).

The function of $Cu(NO_3)_2$ in our process was explored by reacting complex **1** with coordinatively saturated $Cu(acac)_2$ (1:1 molar ratio). ^{31}P NMR monitoring of this reaction mixture revealed that the symmetry and the peak intensity of the $OPPh_3$ ligands in complex **1** were not affected at all by addition of $Cu(acac)_2$. Moreover, the reference OAT reaction (4MTA with TBAN), in which an equimolar mixture of **1** and $Cu(acac)_2$ was used as a catalyst, showed practically the same results as with the complex **1** alone. The dissociation of the $OPPh_3$ ligand was observed by ^{31}P NMR, indicating that a vacant coordination site on the copper metal center has a critical role in improvement of the catalytic process.

Our Mo−Cu catalytic system was further examined as a potential analogue of DMSO reductase,[17] following a literature report regarding the evaluation of a related $MoO_2Cl_2(DMF)_2$ catalyst, as this enzyme analogue.[18] In the latter report, triphenylphosphite underwent oxidation to triphenylphosphate ester, while various sulfoxides were deoxygenated to the corresponding thioethers (Figure 4A).

Guided by this report, we performed a series of reference experiments. We first showed that complex **1** was also capable of promoting the oxidation of PPh_3 with sulfoxides, using 1-methoxy-4-(methylsulfinyl)-benzene or 1-bromo-4-(methylsulfinyl)-benzene as oxidants. We found that in both reactions quantitative conversion of the sulfoxides to the corresponding thioethers was obtained in CH_3CN at 60 °C within 10 h (Figure 4A). In contrast, no traces of thioethers were detected when a mixture of complex **1** with an equivalent amount of $Cu(NO_3)_2$ was used as a catalytic system under the same reaction conditions (Figure 4B). A reference reaction of PPh_3 with complex **1** in the presence of $Cu(NO_3)_2$ (1:1:1 molar ratio) resulted in a complete oxidation of PPh_3 to $OPPh_3$. When the last two control experiments were repeated with coordinatively saturated $Cu(acac)_2$, instead of $Cu(NO_3)_2$, a complete conversion of sulfoxides to the corresponding thioethers was observed (Figure 4C). These results strongly

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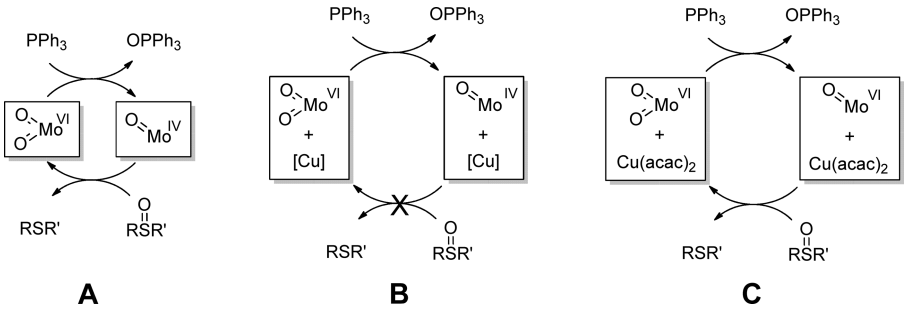

Figure 4. (A) Catalytic oxidation of PPh_3 to $OPPh_3$ with sulfoxides, promoted by $MoO_2Cl_2(DMF)_2$ or complex **1**, as models of the DMSO reductase. (B) "Blocking" catalytic activity of complex **1** in oxidation of PPh_3 by the addition of $Cu(NO_3)_2$ to the reaction mixture. (C) Catalytic oxidation of PPh_3 with sulfoxides, promoted by complex **1** in the presence of $Cu(acac)_2$.

suggest that a copper metal center in the Mo−Cu catalytic system helps to inhibit or block a possible binding of sulfoxide to the molybdenum metal center, thus preventing subsequent reduction of a sulfoxide to thioether.

3. CONCLUSIONS

Analysis of the results of the described above experiments strongly suggests that the presence of the copper metal center in our catalytic system plays a very important role in the found sulfoxidation process. We believe that the copper center is responsible for the effective blocking of the conversion of sulfoxides back to the corresponding thioethers. This process most probably takes place by preventing the coordination of sulfoxides to the molybdenum metal center, thus shifting the sulfoxide−thioether equilibrium. Such an effect was found to be essential for allowing the higher-yield oxidations of thioethers with lower electron density on the sulfur atom.

In summary, we describe an unprecedented catalytic process capable of efficient and highly selective sulfoxidation of thioethers, with the use of nitrate salts as oxidants. This reaction is promoted by a bioinspired Mo−Cu catalytic system, prepared on the basis of complex **1** and a catalytic amount of $Cu(NO_3)_2$. Mild reaction conditions and the use of nitrates as oxidants offer unique advantages of compatibility to a range of functional groups without overoxidation of thioethers to sulfones. This is the first example of high-yield catalytic oxidation of arylthioether boronic acid derivatives with excellent chemoselectivity. These findings greatly expand the existing range of important chemical transformations available for organoboron compounds, providing straightforward accessibility to a variety of new substrates, suitable for Suzuki cross-coupling. Further studies of the reaction mechanism, catalyst structure characterization, and the scope of its activity are in progress.

4. EXPERIMENTAL SECTION

General Experimental Methods. All commercially available reagents and solvents were used as purchased, without further purification. ^{1}H NMR signals were referenced to the residual protons of deuterated solvents. ^{13}C NMR signals were referenced to the carbons of deuterated solvents. ^{31}P NMR signals were to H_3PO_4 (85% in D_2O). Mass spectra were obtained on a spectrometer equipped with CI and EI probes and by GC-MS with a supersonic molecular beam (Supersonic GC-MS).[19] HRMS results were obtained on MALDI-TOF and ESI Q-TOF mass spectrometers.

A single crystal of complex **1** was attached to a glass fiber, with epoxy glue, and transferred to an X-ray diffractometer equipped with a graphite monochromator. Data were collected by using Mo K_α radiation (l = 0.71073 Å). CCDC-781501 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

X-ray Photoelectron Spectroscopy (XPS) measurements were performed in UHV (2.5×10^{-10} Torr base pressure). The sample was irradiated with an Al K_α monochromated source (1486.6 eV), and the outcome electrons were analyzed by a Spherical Capacitor Analyzer using the slit aperture of 0.8 mm. The samples were analyzed at the surface only. Sample charging was compensated by using a charge neutralizer, with additional mathematical shifts referenced to C1s peak energy at 285 eV.

$MoO_2Cl_2(OPPh_3)_2$ (1). To a solution of MoO_2Cl_2 (100 mg, 0.503 mmol) in CH_3CN (20 mL) was added H_2O_2 (9.234 M, 109 μL, 2 equiv). The solution was stirred for 10 min at rt, and when the reaction mixture color changed to orange, PPh_3 (265 mg, 2 equiv) was added. The mixture was stirred for an additional 10 min. Then the stirring was stopped, and the mixture was kept at rt overnight, forming a precipitate. This precipitate was filtered out, washed with diethyl ether (2 × 10 mL), and dried under vacuum to give product **1** as yellow crystals (380 mg, 98%). ^{31}P NMR (80 MHz, CD_3CN) δ 39.8 ppm.

General Procedure for Catalytic Reactions. To a solution of **1** (10 mg, 0.013 mmol, 0.02 equiv) in CH_3CN (5 mL) was added $Cu(NO_3)_2$ (3.2 mg, 0.02 equiv). The mixture was stirred for 5 min at rt. Then a thioether (0.65 mmol, 1 equiv) and tetrabuthylammonium nitrate (198 mg, 0.65 mmol, 1 equiv) were added, and the reaction mixture was stirred at 60 °C overnight. Subsequently, the solvent was evaporated, and the resulted crude product was purified by column chromatography (SiO_2). All reactions were run in duplicates, and when the difference in yields between the two runs was more than 10%, reactions were repeated. The identity of compounds **1**−**4** and compound **6** conformed literature reports.[20]

Phenoxathiin-10-oxide (5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.32 (m, 4H), 7.48−7.52 (m, 2H), 7.80−7.82 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.7, 124.7, 130.9, 133.7, 149.4.

4-(Methylsulfinyl)phenylboronic Acid (11). ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.73 (s, 3 H), 7.63 (d, J = 5.0 Hz, 2H), 7.95 (d, J = 10.0 Hz, 2H), 8.25 (s, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 43.0, 122.4, 134.6, 136.9, 148.0. Mp 165−166 °C. Supersonic GC-MS (EI^+) m/z calcd. for $C_9H_{13}BO_3S$ (M^+): 212.0. Under our analytical conditions, esterification of the boric acid with methanol resulted in formation of $C_9H_{13}BO_3S$. Anal. Calcd for $C_7H_9BO_3S$: C, 45.69; H, 4.93; S, 17.42. Found: C, 45.68; H, 4.88; S, 17.42. IR (KBr): 419, 505, 625, 642, 659, 690, 733, 798, 839, 959, 1010, 1030, 1089, 1167, 1189, 1270, 1350, 1493, 1590, 1594, 3347 cm^{-1}.

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4,4,5,5-Tetramethyl-2-(4-(methylthio)phenyl)-1,3,2-dioxaborolane (12a).[21] A solution of 4-(methylthio)phenylboronic acid (400 mg, 2.38 mmol) and pinacol (281 mg, 2.38 mmol) in toluene (50 mL) was refluxed overnight. Then, molecular sieves (3 Å, 50 mg) were added, and the reaction mixture was stirred for an additional 2 h. After cooling to rt, the reaction mixture was filtered, and the solvent was evaporated to give a pale yellow solid. The residue was purified by column chromatography (SiO_2; *n*-hexane/EtOAc, 2:1) to give **8** as a white solid (560 mg, 94%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.34 (s, 12 H), 2.49 (s, 3H), 7.22 (d, J = 10 Hz, 2H), 7.71 (d, J = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.0, 24.8, 83.7, 125.0, 135.1, 142.5. Anal. Calcd for $C_{13}H_{19}BO_2S$: C, 62.41; H, 7.66. Found: C, 62.09; H, 7.61. Mp 35.1−35.9 °C. IR (KBr): 437, 493, 519, 578, 652, 730, 817, 857, 960, 1018, 1103, 1144, 1211, 1265, 1359, 1394, 1433, 1545, 1596, 2926, 2977 cm^{-1}.

4,4,5,5-Tetramethyl-2-(4-(methylsulfinyl)phenyl)-1,3,2-dioxaborolane (12b). ^{1}H NMR (500 MHz, CD_3CN) δ 1.34 (s, 12 H), 2.67 (s, 3H), 7.64 (d, J = 25.0 Hz, 2H), 7.86 (d, J = 20.0 Hz, 2H). ^{13}C NMR (125 MHz, CD_3CN) δ 25.1, 44.2, 85.2, 110.2, 123.7, 136.0, 150.9. MS (CI$^+$): m/z 267 (MH^+). HRMS (CI$^+$) m/z calcd for $C_{13}H_{20}BO_3S$ (MH^+): 267.1148. Found: 267.1222.

4,4,5,5-Tetramethyl-2-(2-(methylthio)phenyl)-1,3,2-dioxaborolane (13a).[22] A solution of 2-(methylthio)phenylboronic acid (400 mg, 2.38 mmol) and pinacol (281 mg, 2.38 mmol) in toluene (50 mL) was refluxed overnight. Then, molecular sieves (3 Å, 50 mg) were added, and the reaction mixture was stirred for additional 2 h. After cooling to rt, the reaction mixture was filtered, and the solvent was evaporated to give a pale yellow liquid. The residue was purified by column chromatography (SiO_2; *n*-Hexane/EtOAc, 2:1) to give **9** as a colorless liquid (571 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 12 H), 2.45 (s, 3H), 7.10 (dt, J = 1.2 Hz, J = 7.4 Hz, 1H), 7.17 (d, J = 7.6 Hz, 1H), 7.36 (dt, J = 1.6 Hz, J = 7.8 Hz, 1H), 7.68 (dd, J = 1.6 Hz, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.7, 24.8, 83.9, 123.6, 123.8, 131.1, 135.8, 145.1. Supersonic GC-MS (EI$^+$) m/z calcd for $C_{13}H_{19}BO_2S$ (M^+): 250.1. Anal. Calcd. for $C_{13}H_{19}BO_2S$: C, 62.41; H, 7.66; S, 12.82. Found: C, 62.60; H, 7.54; S, 12.30. Mp 77.5−78.6 °C. IR (KBr): 498, 576, 652, 698, 737, 764, 823, 856, 957, 1046, 1103, 1139, 1206, 1257, 1347, 1379, 1432, 1468, 1560, 1584, 2922, 2975, 3061 cm^{-1}.

4,4,5,5-Tetramethyl-2-(2-(methylsulfinyl)phenyl)-1,3,2-dioxaborolane (13b). ^{1}H NMR (500 MHz, CD_3CN) δ 1.33 (s, 12 H), 2.69 (s, 3H), 7.51 (t, J = 5.0 Hz, 1H), 7.68 (t, J = 10.0 Hz, 1H), 7.77 (d, J = 5.0 Hz, 1H), 7.93 (J = 5.0 Hz, 1H). ^{13}C NMR (125 MHz, CD_3CN) δ 25.2, 44.8, 85.4, 123.2, 130.8, 132.7, 136.3, 153.8. MS (CI$^+$): m/z 267 (MH^+). Mp 59.0−60.2 °C. IR (KBr): 513, 543, 647, 699, 741, 767, 800, 856, 965, 1026, 1095, 1144, 1262, 1353, 1431, 1474, 1590, 1652, 2361, 2966, 3049 cm^{-1}.

(3*aR*,7*aS*)-2-(4-(Methylthio)phenyl)hexahydrobenzo-[d]-[1,3,2]dioxaborole (14a). A solution of 4-(methylthio)phenylboronic acid (400 mg, 2.38 mmol) and (1*R*,2*S*)-1,2-cyclohexanediol (276 mg, 2.38 mmol) in toluene (50 mL) was refluxed overnight. Then, molecular sieves (3 Å, 50 mg) were added, and the reaction mixture was stirred for an additional 2 h. After cooling to rt, the reaction mixture was filtered, and the solvent was evaporated to give a pale yellow solid. The residue was purified by column chromatography (SiO_2; *n*-hexane/EtOAc, 2:1) to give **10** as a white solid (578 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38−1.41 (m, 2 H), 1.57−1.61 (m, 2H), 1.81−1.88 (m, 4H), 2.49 (s, 3H), 4.52 (m, 2H), 7.25 (d, J = 8 Hz, 2H), 7.74 (d, J = 12.0, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 18.9, 28.3, 75.2, 124.6, 134.8, 142.5. MS (CI$^+$): m/z 249 (MH^+). HRMS (CI$^+$) calcd for $C_{13}H_{17}BO_2S$ (MH^+): 249.1121. Found: 249.1100.

(3*aR*,7*aS*)-2-(4-(Methylsulfinyl)phenyl)hexahydrobenzo-[d]-[1,3,2]dioxaborole (14b). This compound was not stable enough to undergo a column chromatography or any other examined purification technique. The yield was estimated by ^{1}H NMR integration of peaks of the product and the starting material. Only one product was observed by NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38−1.41 (m, 2H), 1.57−1.61 (m, 2H), 1.81−1.88 (m, 4H), 2.73 (s, 3H), 4.71 (m, 2H), 7.58 (d, J = 8 Hz, 2H), 7.88 (d, J = 12.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 29.2, 44.3, 76.0, 126.0, 136.1, 144.0.

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures, synthesis of substrates, ^{1}H NMR, ^{13}C NMR, and ^{31}P NMR, XPS, mass spectrometry, FT-IR, and X-ray crystallography data. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ REFERENCES

(1) (a) Lane, B. S.; Burgess, K. *Chem. Rev.* **2003**, *103*, 2457–2473. (b) Nugent, W. A.; RajanBabu, T. V.; Burk, M. J. *Science* **1993**, *259*, 479–483. (c) Veiros, L. F.; Prazeres, Â.; Costa, P. J.; Romão, C. C.; Kühn, F. E.; Calhorda, M. J. *Dalton Trans.* **2006**, *11*, 1383–1389. (d) Güenyar, A.; Betz, D.; Drees, M.; Herdtweck, E.; Kühn, F. E. *J. Mol. Catal. A: Chem.* **2010**, *331*, 117–124.

(2) (a) Coughlan, M. P. *Molybdenum and Molybdenum-Containing Enzymes*; Pergamon Press: New York, 1980. (b) Spiro, T. G. *Molybdenum Enzymes*; Wiley-Interscience: New York, 1985. (c) Hille, R. *Chem. Rev.* **1996**, *96*, 2757–2816. (d) Romao, M. J.; et al. *Structure* **1999**, *7*, 65–79. (e) Güenter, S.; Mendel, R. R.; Ribbe, M. W. *Nature* **2009**, *460*, 839–847.

(3) (a) Holm, R. H. *Chem. Rev.* **1987**, *87*, 1401–1449. (b) Nagarajan, K.; Joshi, H. K.; Chaudhury, K.; Pal, K.; Cooney, J. J. A.; Enemark, J. H.; Sarkar, S. *Inorg. Chem.* **2004**, *43*, 4532–4533. (c) Enemark, J. H.; Cooney, J. J. A.; Wang, J.; Holm, R. H. *Chem. Rev.* **2004**, *104*, 1175–1200.

(4) (a) Kail, B. W.; Perez, L. M.; Zaric, S. D.; Millar, A. J.; Young, C. G.; Hall, M. B.; Basu, P. *Chem.—Eur. J.* **2006**, *12*, 7501–7509. (b) Smith, P. D.; Millar, A. J.; Young, C. G.; Ghosh, A.; Basu, P. *J. Am. Chem. Soc.* **2000**, *122*, 9298–9299. (c) Nemykin, V. N.; Laskin, J.; Basu, P. *J. Am. Chem. Soc.* **2004**, *126*, 8604–8605. (d) Millar, A. J.; Doonan, C. J.; Smith, P. D.; Nemykin, V. N.; Basu, P.; Young, C. G. *Chem.—Eur. J.* **2005**, *11*, 3255–3267. (e) Sengar, R. S.; Nemykin, V. N.; Basu, P. *J. Inorg. Biochem.* **2008**, *102*, 748–756.

(5) (a) Gasparrini, F.; Giovannoli, M.; Misiti, D.; Natile, G.; Palmieri, G. *Tetrahedron* **1983**, *39*, 3181–3184. (b) Yuan, Y.; Bian., Y. *Tetrahedron Lett.* **2007**, *48*, 8518–8520.

(6) (a) Komatsu, N.; Uda, M.; Suzuki, H. *Chem. Lett.* **1997**, 1229–1230. (b) Komatsu, N.; Taniguchi, A.; Wada, S.; Suzuki, H. *Adv. Synth. Catal.* **2001**, *343*, 473–480.

(7) (a) Holland, H. L. *Chem. Rev.* **1988**, *88*, 473–485. (b) Block, E. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1135–1178.

(8) (a) Jones, C. W. *Application of Hydrogen Peroxide and Derivatives*; MPG Books Ltd.: Cornwall, UK, 1999. (b) Adam, W. *Peroxide Chemistry*

Mechanistic and Preparative Aspects of Oxygen Transfer; Wiley−VCH: Darmstadt, Germany, 2000.

(9) (a) Hudlicky, M. *ACS Monogr.* **1990**, 433. (b) Procter, D. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 641–668. (c) Mata, E. G. *Phosphorus, Sulfur Silicon Relat. Elem.* **1996**, *117*, 231–286. (d) Madesclaire, M. *Tetrahedron* **1986**, *42*, 5459–5495.

(10) (a) Caron, S.; Dugger, R. W.; Ruggeri, S. G.; Ragan, J. A.; Ripin, D. H. *Chem. Rev.* **2006**, *106*, 2943–2989. (b) Sato, K.; Hyodo, M.; Aoki, M.; Zheng, X.-Q.; Noyori, R. *Tetrahedron* **2001**, *57*, 2469–2476. (c) Fraile, J. M.; Lazaro, B.; Mayoral, J. A. *Chem. Commun.* **1998**, 1807–1808.

(11) (a) Thiel, W. R.; Barz, M.; Glas, H.; Pleier, A. K. *Peroxide Chem.* **2000**, 433–453. (b) Sharpless, K. B.; Townsend, J. M.; Williams, D. R. *J. Am. Chem. Soc.* **1972**, *94*, 295–296. (c) Lane, B. S.; Burgess, K. *Chem. Rev.* **2003**, *103*, 2457–2473.

(12) (a) Gago, S.; Neves, P.; Monteiro, B.; Pessêgo, M.; Lopes, A. D.; Valente, A. A.; Almeida Paz, F. A.; Pillinger, M.; Moreira, J.; Silva, C. M.; Goncalves, I. S. *Eur. J. Inorg. Chem.* **2009**, 4528–4537. (b) Veiros, L. F.; Prazeres, A.; Costa, P. J.; Romão, C. C.; Kühn, F. E.; Calhorda, M. *J. Dalton Trans.* **2006**, 1383–1389. (c) Groarke, M.; Goncalves, I. S.; Herrmann, W. A.; Kühn, F. E. *J. Organomet. Chem.* **2002**, *649*, 108–112. (d) Kühn, F. E.; Santos, A. G.; Lopes, A. D.; Goncalves, I. S.; Rodríguez-Borges, J. E.; Pillinger, M.; Romão, C. C. *J. Organomet. Chem.* **2001**, *621*, 207–217.

(13) (a) Butcher, R. J.; Penfold, B. R.; Sinn, E. *J. Chem. Soc., Dalton Trans.* **1979**, *4*, 668–675. (b) Wang, G.; Chen, G.; Luck, R. L.; Wang, Z.; Mu, Z.; Evans, D. G.; Duan, X. *Inorg. Chim. Acta* **2004**, *357*, 3223–3229.

(14) Chatt, J.; Elson, C. M.; Leigh, G. J.; Connor, J. A. *J. Chem. Soc., Dalton Trans.* **1976**, *14*, 1351–1354.

(15) (a) Klein, R.; Friedel, R. A. *J. Am. Chem. Soc.* **1950**, *72*, 3810–3811. (b) Kool, D. M.; Wrage, N.; Oenema, O.; Dolfing, J.; Van Groenigen, J. W. *Rapid Commun. Mass Spectrom.* **2007**, *21*, 3569–3578.

(16) Kinen, C. O.; Rossi, L. I.; De Rossi, R. H. *J. Org. Chem.* **2009**, *74*, 7132–7139.

(17) Hille, R. *Chem. Rev.* **1996**, *96*, 2757–2816.

(18) Holm, R. H. *Coord. Chem. Rev.* **1990**, *100*, 183–221.

(19) Amirav, A.; Gordin, A.; Poliak, M.; Fialkov, A. B. *J. Mass. Spectrom* **2008**, *43*, 141–163.

(20) (a) Ali, M. H. *Synthesis* **2007**, 3507–3511. (b) Caupene, C. *J. Org. Chem.* **2005**, *70*, 2812–2815. (c) Foucoin, F. *Synthesis* **2007**, 1315–1324. (d) Gao, Y. *Adv. Synth. Catal.* **2008**, *350*, 2937–2946.

(21) (a) Claudel, S.; Gosmini, C.; Paris, J. M.; Périchon, J. *Chem. Commun.* **2007**, *35*, 3667–3669. (b) Spencer, J. *ACS Comb. Sci.* **2011**, *13*, 24–31.

(22) Claudel, S. *Chem. Commun.* **2007**, 3667–3669.