

Reduction of sulfoxides with boranes catalyzed by MoO_2Cl_2

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Abstract—The first example of an organic reduction with boranes catalyzed by a high valent oxo-complex is reported. The systems catecholborane/ $\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$ (5 mol %) and $\text{BH}_3\cdot\text{THF}/\text{MoO}_2\text{Cl}_2$ (5 mol %) proved to be very efficient for the reduction of sulfoxides to the corresponding sulfides in excellent yields.

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High valent dioxomolybdenum(VI) complexes are known for their abilities to catalyze oxygen-transfer reactions to sulfides, phosphines and olefins.^{1–5} Recently, we have demonstrated the reversal of the role of MoO_2Cl_2 (**1**) by showing its ability to catalyze organic reductions.^{6–10} In our previous works, we have shown that MoO_2Cl_2 activates the Si–H bond of different silanes such as PhSiH_3 , $\text{Ph}(\text{Me})_2\text{SiH}$, Et_3SiH and PMHS and that the system silane/ MoO_2Cl_2 is very efficient for the hydrosilylation of aldehydes and ketones, yielding the corresponding silyl ethers⁶ and for the reduction of imines,⁷ amides,⁸ esters,⁹ sulfoxides¹⁰ and pyridine *N*-oxides¹⁰ to the corresponding amines, alcohols, sulfides and pyridines (see Scheme 1).

Our interest in the study of the catalytic activity of this high valent oxo-complex led us to explore the activation of B–H bond of boranes and the use of the catalytic system borane/ MoO_2Cl_2 in organic reductions, particularly, in the reduction of sulfoxides.

The deoxygenation of sulfoxides to the corresponding sulfides is an important organic and biological reaction. Over the years, several methods have been developed to reduce sulfoxides.^{11–18} However, since many of these transformations are limited by side reactions, low yields,

lack of chemoselectivity or harsh conditions, a search for new catalysts remains justifiable.

In the literature, there are only few examples of the reduction of sulfoxides with boron reagents such as the xylchloroborane-methyl sulfide,¹⁹ dichloroborane²⁰ and tribromoborane,²¹ but the difficulty in handling these highly reactive reagents makes their use somewhat impracticable.

Catecholborane (HBcat) is one of the most versatile boron hydride reagents available to the synthetic chemist. This borane is stable in dry air and may be stored unchanged for over a year at 0 °C, in contrast to certain other substituted boranes.

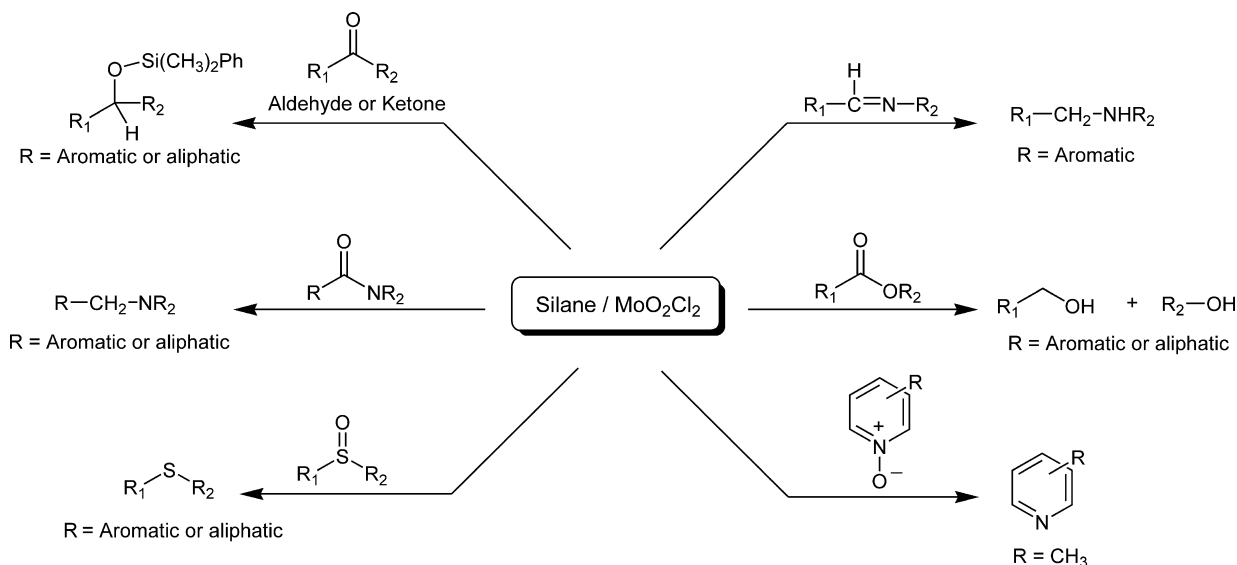
Westcott¹⁶ described the reduction of sulfoxides with 3 equiv of HBcat at room temperature in quantitative yields. However, with aromatic substrates these reductions required longer reaction times, for example, the deoxygenation of phenyl sulfoxide or 4-chlorophenyl sulfoxide required more than 500 h. These authors also described the acceleration of this reduction upon the addition of rhodium catalysts such as $\text{RhCl}(\text{PPh}_3)_3$ and $\text{Rh}(\text{acac})(\text{dppe})$.

In this Letter, we investigated the activation of boranes by dioxomolybdenum dichloride and the deoxygenation of aromatic sulfoxides with the systems HBcat/ $\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$ and $\text{BH}_3\cdot\text{THF}/\text{MoO}_2\text{Cl}_2$.

The reduction of sulfoxides was initially studied with 2 equiv of HBcat in THF in the presence of 5 mol %

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Scheme 1. Organic reductions with the system silane/ MoO_2Cl_2 .

of a diethyl ether solution of $\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$, at reflux temperature and under air atmosphere, as summarized in Table 1.²² These reductions were very fast (15–35 min), and the corresponding sulfides were obtained in excellent yields (Table 1, entries 1, 3, 5, 7, 9 and 11).

Table 1. Reduction of sulfoxides with the system $\text{HBcat}/\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$

Entry	Sulfoxide	Temp (°C)	Time	Yield ^b (%)
1		67	25 min	93
2		rt	16 h	91
3		67	30 min	95
4		rt	16 h	91
5		67	30 min	92
6		rt	16 h	89
7		67	30 min	93
8		rt	16 h	89
9		67	35 min	89
10		rt	16 h	85
11		67	15 min	94
12		rt	16 h	88

^a All reactions were carried out with 1.0 mmol of sulfoxide, 2 mmol of HBcat and 5 mol % of $\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$.

^b Isolated yield.

To verify if the catalyst has an active role in the deoxygenation, all the reactions were carried out without catalyst with the addition of 2 equiv of HBcat . Under these conditions, the yields of sulfides were either very low or the reactions did not occur.

When the reductions were carried out with 1.2 equiv of HBcat , the sulfides were also obtained in low yields. At room temperature, the reactions required significantly longer reaction times (Table 1, entries 2, 4, 6, 8, 10 and 12).

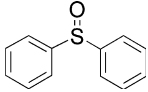
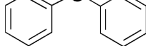
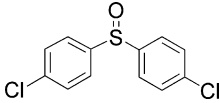
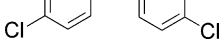
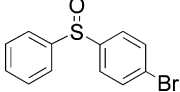
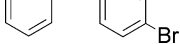
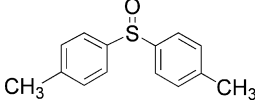

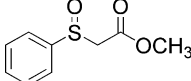
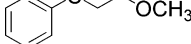
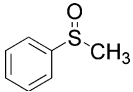

This novel method is compatible with halo and ester groups (Table 1, entries 3–6, 9 and 10). However, the analysis of the ^1H NMR spectrum of the reaction mixture obtained in the reduction of the phenyl vinyl sulfoxide with the system $\text{HBcat}/\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$ showed that the double bond was affected.

The reusability of $\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$ was evaluated using 4-chlorophenyl sulfoxide as test substrate. We carried out five successive reactions by sequential addition of fresh substrate and HBcat to the reaction mixture. The catalytic activity of $\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$ was followed by ^1H NMR, and after each 30 min at reflux temperature, we observed the complete reduction of sulfoxide. This result showed that the catalytic activity of $\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$ did not decrease with successive uses.

We also investigated the reduction of sulfoxides with the system $\text{BH}_3\cdot\text{THF}/\text{MoO}_2\text{Cl}_2$ in refluxing THF under nitrogen atmosphere.²³ From the analysis of Table 2, we concluded that the system $\text{BH}_3\cdot\text{THF}/\text{MoO}_2\text{Cl}_2$ is also very efficient for the reduction of sulfoxides and these results are very similar to those obtained with the system $\text{HBcat}/\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$. This catalytic system is compatible with halo and ester substituents (Table 2, entries 3–6, 9 and 10).

The use of $\text{HBcat}/\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$ has some practical advantages associated with the borane and the catalyst.

Table 2. Reduction of sulfoxides with the system $\text{BH}_3\cdot\text{THF}/\text{MoO}_2\text{Cl}_2$ ^a

$\text{R}_1-\overset{\text{O}}{\parallel}{\text{S}}-\text{R}_2 \xrightarrow[\text{THF}]{\text{BH}_3\cdot\text{THF} / \text{MoO}_2\text{Cl}_2 (5 \text{ mol}\%)} \text{R}_1-\text{S}-\text{R}_2$				
Entry	Sulfoxide	Temp (°C)	Time	Yield ^b (%)
1		67	25 min	91
2		rt	16 h	88
3		67	30 min	92
4		rt	16 h	89
5		67	25 min	90
6		rt	16 h	87
7		67	30 min	91
8		rt	16 h	88
9		67	35 min	88
10		rt	16 h	85
11		67	10 min	93
12		rt	16 h	87

^a All reactions were carried out with 1.0 mmol of sulfoxide, 2.0 mmol of $\text{BH}_3\cdot\text{THF}$ and 5 mol % of MoO_2Cl_2 .

^b Isolated yield.

Catecholborane is more stable and easily handled than $\text{BH}_3\cdot\text{THF}$, and the complex $\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$ is easily and inexpensively prepared by extraction from a hydrochloric acid solution of Na_2MoO_4 with diethyl ether,²⁴ in contrast to the difficult preparation of MoO_2Cl_2 . Other important advantage is related to the air stability of the ether solution of $\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$, which enables the reaction to be carried out under air atmosphere.

As observed in our previous catalytic system, silane/ MoO_2Cl_2 , attempted reduction of phenyl sulfone and

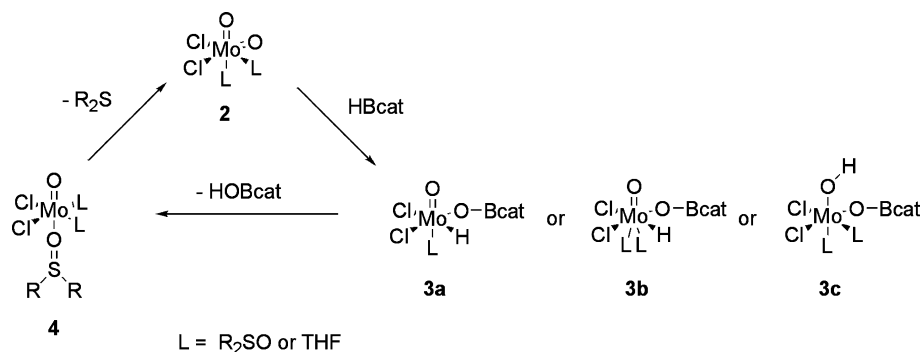
4-fluorophenyl methyl sulfone with $\text{BH}_3\cdot\text{THF}/\text{MoO}_2\text{Cl}_2$ or $\text{HBcat}/\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$ resulted in the recovery of the starting material.

The analysis of Tables 1 and 2 shows that the presence of MoO_2Cl_2 is essential for the efficient reduction of sulfoxides. We suggest that the mechanism for the deoxygenation of sulfoxide with the catalytic system $\text{HBcat}/\text{MoO}_2\text{Cl}_2(\text{H}_2\text{O})_2$ starts with the activation of the sulfoxide by the oxygen coordination to the molybdenum, yielding the complex $\text{MoO}_2\text{Cl}_2(\text{sulfoxide})_2$. This complex weakens the S–O bond and renders the sulfur atom more susceptible to the reduction.

As mentioned above, Si–H bonds are activated by $\text{Mo}=\text{O}$ and other $\text{Re}=\text{O}$ complexes leading to hydrosilylation and other reduction reactions. In the case of MoO_2Cl_2 , computational DFT studies do not distinguish clearly between the so-called [2+2] and [3+2] addition modes, depicted in Scheme 2. No such studies have yet been carried out for the interaction between boranes and MoO_2Cl_2 . However, the Lewis-acidic character of the boranes will most likely assist B–H bond breaking on this complex via the coordination of one oxo ligand to the vacant orbital on the boron. Such process will be even more favoured in a sulfoxide complex like $(\text{R}_2\text{SO})_2\text{MoO}_2\text{Cl}_2$ (**4**), where the $\text{Mo}=\text{O}$ bond is weakened by the electronic competition from the trans sulfoxide ligands. Of course, under catalytic reaction conditions where a vast excess of the sulfoxide is present relative to the MoO_2Cl_2 , a sulfoxide like **4** is almost inevitably present at the outset of the reaction.

With this in mind, Scheme 2 depicts our proposed reaction mechanism for the catalytic deoxygenation of sulfoxides by HBcat .

Intermediates **3a** and **3b** result from the [2+2] addition of the B–H bond to one $\text{Mo}=\text{O}$ bond while **3c** represents the result of the [3+2] addition. While they are readily interconvertible for the $\text{MoO}_2\text{Cl}_2/\text{H}-\text{SiR}_3$ addition,²⁵ we cannot say the same for the present situation. However, HOBCat elimination would, in both cases, lead to the same species **4**. This $\text{Mo}(\text{IV})$ complex is very well known to cleave the $\text{S}=\text{O}$ bond²⁶ leading to the final thioether R_2S and reforming the initial species **2**. The HOBCat can react with another molecule of HBcat giving catBOBCat and hydrogen. The formation of

**Scheme 2.**

catBOBcat is supported by the need of 2 equiv of HBcat to achieve good yields.

To the best of our knowledge, this is the first example of the B–H bond activation by high valent oxo-complexes. Catalyzed reactions with boranes reported in the literature usually involve transition metal complexes in a low oxidation state.^{27–30}

These results confirm the new role of MoO₂Cl₂ as an excellent catalyst for X–H (X = Si and B) bond activation.

In summary, we have developed a novel method for the reduction of sulfoxides using the systems HBcat/MoO₂Cl₂(H₂O)₂ and BH₃·THF/MoO₂Cl₂ in excellent yields. This work showed that MoO₂Cl₂ activates the B–H bond and can be used as catalyst for reductions with boranes. These results suggest several future applications of the system borane/MoO₂Cl₂, since reductions with boranes are among the most important synthetic methodologies in organic chemistry.

The scope of these novel catalytic systems is now under investigation in our group.

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- In a typical experiment, to the mixture of sulfoxide (1.0 mmol) and the diethyl ether solution of MoO₂Cl₂(H₂O)₂ (5 mol %) the solution of catecholborane was added in THF (2.0 mmol). The reaction mixture was stirred under air atmosphere (the temperature and the reaction times are indicated in Table 1) and the progress of the reaction was monitored by TLC and ¹H NMR. Upon completion, the reaction mixture was evaporated and purified by silica gel column chromatography with the appropriate mixture of *n*-hexane and ethyl acetate to afford the sulfides, which are all known compounds.
- In a typical experiment, to a solution of MoO₂Cl₂ (5 mol %) in THF (3 ml) was added the sulfoxide (1.0 mmol) and the solution of BH₃·THF in THF (2.0 mmol). The reaction mixture was stirred under nitrogen atmosphere (the temperature and the reaction times are indicated in Table 2) and the progress of the reaction was monitored by TLC and ¹H NMR. Upon completion, the reaction mixture was evaporated and purified by silica gel column chromatography with the appropriate mixture of *n*-hexane and ethyl acetate to afford the sulfides, which are all known compounds.
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