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Highly efficient and chemoselective reduction of sulfoxides using the system silane/oxo-rhenium complexes

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ABSTRACT

This work reports a novel method for the reduction of sulfoxides with silanes catalyzed by high valent oxo-rhenium(V) and (VII) complexes. The catalytic system $PhSiH_3/ReIO_2(PPh_3)_2$ (1 mol %) proved to be highly efficient for the reduction of a wide range of sulfoxides in excellent yields under mild conditions. This novel methodology is also highly chemoselective, tolerating several functional groups such as –CHO, $–CO_2R$, –Cl, $–NO_2$, and double or triple bonds.

The reduction of sulfoxides to the corresponding sulfides is an important reaction that has found utility in organic synthesis and in biochemical reactions. Over the years, several methods have been developed to reduce sulfoxides,[1–25] however, many of these are limited by side reactions, low yields, lack of chemoselectivity, or harsh conditions. For example, the use of hydrogen halides is somewhat restricted with acid-sensitive substrates, the reductions with the strong hydride systems $LiAlH_4–TiCl_4$ and $NaBH_4–CoCl_2$ are incompatible with several functional groups, and the reactions with phosphorous reagents, in most cases, require elevated temperature and/or prolonged reaction times. Due to the high importance of selective reduction of sulfoxides, the search for alternative efficient and highly chemoselective methods remains an important target in organic synthesis.

Recently, we have demonstrated that high valent oxo-molybdenum and -rhenium complexes were excellent catalysts for X–H bond activation and for organic reactions.[26–32] We also reported the deoxygenation of sulfoxides with silanes[33] and boranes[34] catalyzed by MoO_2Cl_2 in excellent yields.

In this work we have studied the reduction of sulfoxides with silanes catalyzed by a series of high valent oxo-rhenium(V) and (VII) complexes.

In order to optimize the reaction conditions, firstly we studied the reduction of the test substrate 4-chlorophenyl sulfoxide catalyzed by 1 mol % of high valent oxo-rhenium complexes $ReIO_2(PPh_3)_2$, $ReOCl_3(PPh_3)_2$, Re_2O_7, MTO, and $ReOCl_3$(dppm), with different silanes (100 mol %), and using several solvents (Tables 1–3). The progress of the reactions was monitored by thin layer chromatography and by ^1H NMR.

Among the oxo-rhenium complexes tested, $ReIO_2(PPh_3)_2$ was the most effective catalyst, reducing completely the 4-chlorophenyl sulfoxide in 5 min in THF at room temperature (Table 1, entry 1). The complex $ReOCl_3(PPh_3)_2$ was also an excellent catalyst for this reaction, giving the sulfide in 100% conversion after 15 min (Table 1, entry 2). The deoxygenations carried out with Re_2O_7, MTO, and $ReOCl_3$(dppm) also completely reduced the sulfoxide, but the reactions were much slower, taking 16–24 h (Table 1, entries 3–5). Finally, in the absence of catalyst no product was detected after 1 day (Table 1, entry 6).

The reduction of 4-chlorophenyl sulfoxide performed with the silanes $PhSiH_3$, PMHS, $PhMe_2SiH$, Et_3SiH, and Ph_3SiH (100 mol %), catalyzed by 1 mol % of $ReIO_2(PPh_3)_2$, showed that $PhSiH_3$ was the most efficient reagent, reducing completely the 4-chlorophenyl sulfoxide in 5 min in THF at room temperature (Table 2, entry 1). However, using only 33 mol % of $PhSiH_3$, the reaction afforded the sulfide in only 50% conversion after 24 h (Table 2, entry 2). The deoxygenation carried out with polymethylhydrosiloxane (PMHS) also gave the sulfide in 100% conversion, but the reaction required 15 h (Table 2, entry 3). In contrast, the reactions performed with $PhMe_2SiH$, Et_3SiH, and Ph_3SiH at room temperature afforded the sulfide in moderate conversions (Table 2, entries 4, 6, and 8). At reflux temperature, the reduction with $PhMe_2SiH$ is completed after 24 h (Table 2, entry 5).

This method was also studied with different solvents. Tetrahydrofuran was the best solvent for the reduction of 4-chlorophenyl sulfoxide with $PhSiH_3$ catalyzed by $ReIO_2(PPh_3)_2$, affording the product in 100% conversion in only 5 min at room temperature

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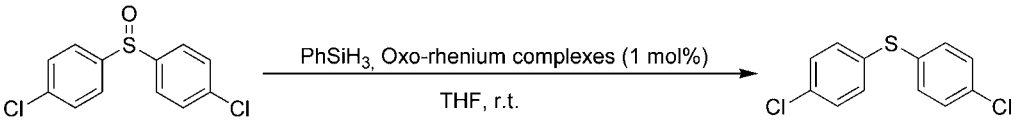
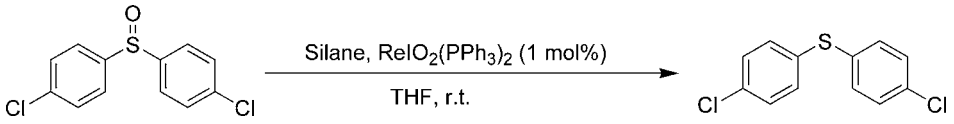
Table 1
Reduction of 4-chlorophenyl sulfoxide with phenylsilane catalyzed by high valent oxo-rhenium complexes[a]



Entry	Catalyst	Time	Conversion[b] (%)
1	$ReIO_2(PPh_3)_2$	5 min	100
2	$ReOCl_3(PPh_3)_2$	15 min	100
3	Re_2O_7	16 h	100
4	MTO	22 h	100
5	$ReOCl_3$(dppm)	24 h	100
6	Without catalyst	24 h	No reaction

[a] The reactions were carried out with 0.5 mmol of sulfoxide, 100 mol % of silane and 1 mol % of catalyst.
[b] Conversion was determined by ^{1}H NMR.

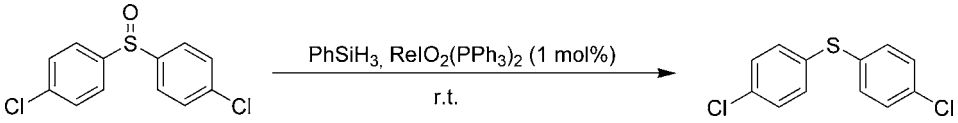
Table 2
Reduction of 4-chlorophenyl sulfoxide with different silanes catalyzed by $ReIO_2(PPh_3)_2$[a]



Entry	Silane	Silane (mol %)	Temperature	Time	Conversion[b] (%)
1	$PhSiH_3$	100	rt	5 min	100
2	$PhSiH_3$	33	rt	24 h	50
3	PMHS	0.30	rt	15 h	100
4	$PhMe_2SiH$	100	rt	24 h	50
5	$PhMe_2SiH$	100	Reflux	24 h	100
6	Et_3SiH	100	rt	24 h	30
7	Et_3SiH	100	Reflux	24 h	40
8	Ph_3SiH	100	rt	24 h	47

[a] All reactions were carried out with 0.5 mmol of sulfoxide and 1 mol % of $ReIO_2(PPh_3)_2$.
[b] Conversion was determined by ^{1}H NMR.

Table 3
Reduction of 4-chlorophenyl sulfoxide in different solvents[a]



Entry	Solvent	Time	Conversion[b] (%)
1	THF	5 min	100
2	CH_2Cl_2	15 min	100
3	Toluene	25 min	100
4	$CHCl_3$	1 h 30 min	100
5	Benzene	7 h 30 min	100
6	CH_3CN	24 h	10

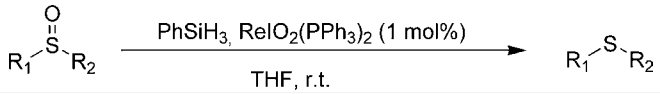
[a] All reactions were carried out with 0.5 mmol of sulfoxide, 100 mol % of $PhSiH_3$, 1 mol % of $ReIO_2(PPh_3)_2$.
[b] Conversion was determined by ^{1}H NMR.

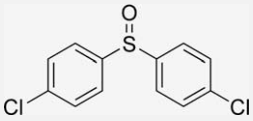
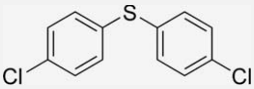
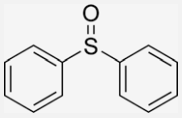
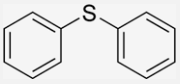
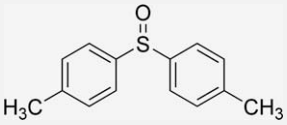
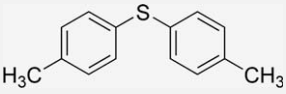
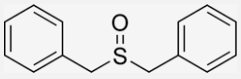
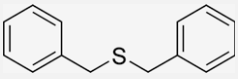
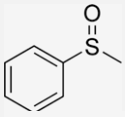
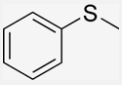
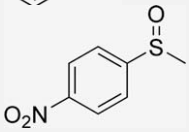
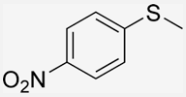
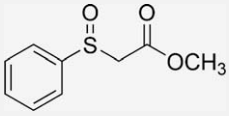
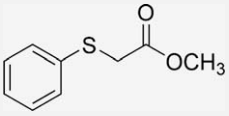
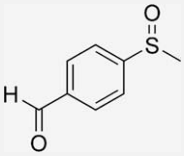
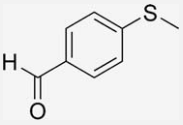
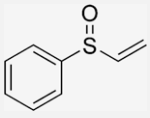
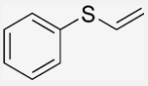
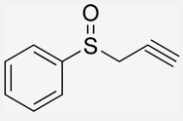
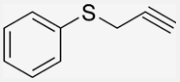
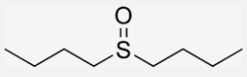
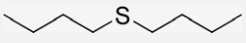
(Table 3, entry 1). Dichloromethane, chloroform, and toluene were also good solvents, giving the sulfide within 15–90 min (Table 3, entries 2–4). In contrast, the complete deoxygenation of 4-chlorophenyl sulfoxide performed in benzene required several hours (Table 3, entry 5) and in acetonitrile only 10% conversion of product was obtained after 1 day (Table 3, entry 6).

To assess the scope and limitations of this novel methodology, we carried out the reduction of several sulfoxides bearing other potentially labile functional groups with the catalytic system $PhSiH_3/ReIO_2(PPh_3)_2$ (1 mol %).[35] These reactions were performed with 1.0 mmol of substrate in THF at room temperature under air atmosphere. As shown in Table 4, this methodology is equally applicable to diaryl, aryl alkyl, and dialkyl sulfoxides. The efficiency of the catalytic system $PhSiH_3/ReIO_2(PPh_3)_2$ is also demonstrated by the good yield obtained in the reduction of dibenzyl sulfoxide (Table 4, entry 4), since several methods fail completely with this substrate or only provide poor yields.

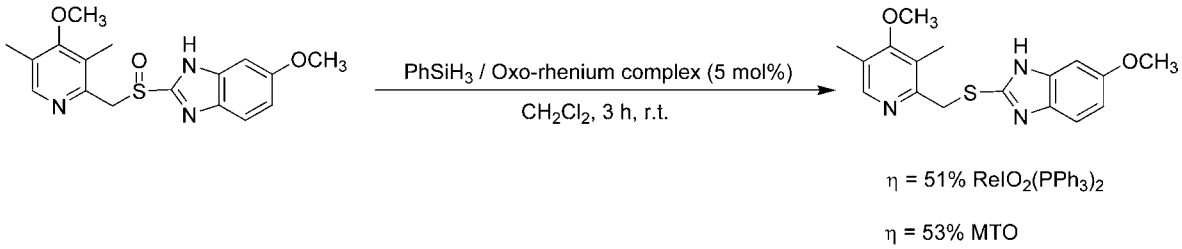
The high chemoselectivity of this method is evident from entries 1, 6–11 of Table 4, which show that –Cl, $-NO_2$, $-CO_2R$, –CHO, and double or triple bond functionalities are unaffected under the reaction conditions. Remarkable is the chemoselective reduction of the sulfinyl group observed in the substrate of entry

Table 4
Reduction of sulfoxides with the catalytic system $PhSiH_3/ReIO_2(PPh_3)_2$[a]



Entry	Substrate	Product	Time	Yield[b] (%)
1			30 min	96
2			20 min	97
3			25 min	95
4			30 min	83
5			10 min	91
6			15 min	90
7			25 min	94
8			2 h 15 min	92[c]
9			35 min	81
10			24 h	71
11			40 min	80[d]
12			15 min	100[e]

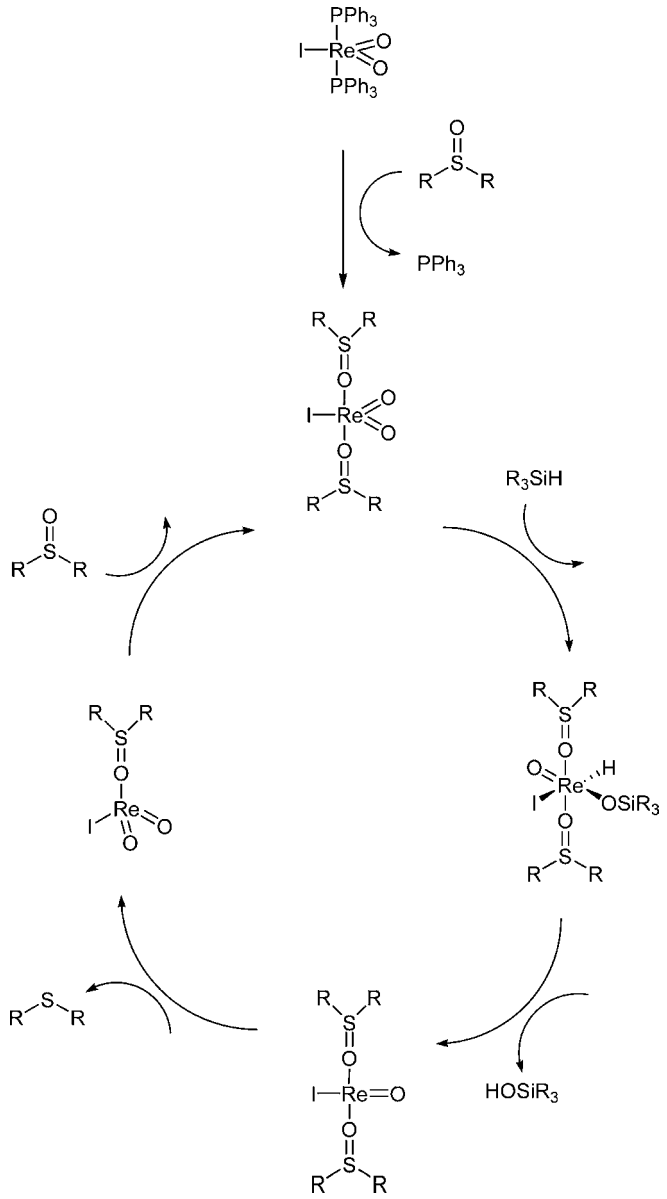
[a] The reactions were carried out with 1.0 mmol of sulfoxide, 100 mol % of $PhSiH_3$, 1 mol % of $ReIO_2(PPh_3)_2$, and 3 mL of the solvent.
[b] Isolated yields.
[c] This reaction was carried out adding slowly 33 mol % of $PhSiH_3$.
[d] This reaction was carried out at reflux temperature.
[e] Conversion was determined by ^1H NMR.



Scheme 1. Reduction of omeprazole using the catalytic system $PhSiH_3$/oxo-rhenium complexes.

8, adding slowly 33 mol % of $PhSiH_3$, in which the carbonyl group remained intact. Using 100 mol % of this silane, we observed the reduction of both functional groups.

This novel methodology was also applied to the reduction of anti-ulcer drug omeprazole (Scheme 1). The reduction was performed with the catalytic systems $PhSiH_3$ (200 mol %)/$ReIO_2(PPh_3)_2$ (5 mol %) and $PhSiH_3$ (100 mol %)/MTO (5 mol %) in dichloromethane at room temperature under air atmosphere, affording the corresponding sulfide in moderate yields.



Scheme 2. Proposed catalytic cycle for the reduction of sulfoxides with the system silane/$ReIO_2(PPh_3)_2$ (1 mol %).

Comparing this novel method with our previous catalytic system $PhSiH_3/MoO_2Cl_2$ (5 mol %),[33] we conclude that the reactions performed with the system $PhSiH_3/ReIO_2(PPh_3)_2$ (1 mol %) are much faster and can be carried out at room temperature under air atmosphere, using less amount of catalyst.

Mechanistically, we suggest the initial substitution of the phosphine by the sulfoxides, affording the complex $ReIO_2(R_2SO)_2$ (see Scheme 2). In the second step, the hydride species $(R_2SO)_2(O)IRe(H)OSiR_3$ is formed as a result of the addition of the Si–H bond of the silane to one of the oxo-rhenium bonds. This reaction is similar to the formation of the hydride $(PPh_3)_2(O)IRe(H)OSiMe_2Ph$ reported by Toste and co-workers,[36,37] reacting $ReIO_2(PPh_3)_2$ with $PhMe_2SiH$.

In the next step, a molecule of $HOSiR_3$ is eliminated, giving the monoxo-rhenium(III) complex $ReI(O)(R_2SO)_2$. This complex can easily rearrange to liberate the sulfide R_2S and reform the species $ReIO_2(R_2SO)$. Finally, the latter will be stabilized by the entry of another molecule of sulfoxide regenerating the dioxo-rhenium complex $ReIO_2(R_2SO)_2$.

In conclusion, we have demonstrated that oxo-rhenium(V) and (VII) complexes are excellent catalysts for the reduction of several sulfoxides with silanes. This novel methodology is highly chemoselective, tolerating a large range of functional groups such as –CHO, $–CO_2R$, –Cl, $–NO_2$, and double or triple bonds. This method was applied in the deoxygenation of aromatic and aliphatic sulfoxides and also in the reduction of the anti-ulcer drug omeprazole.

Other advantages of this procedure include high isolated yields, low catalyst loading (1 mol %), fast and clean reactions, mild reaction conditions, simple experimental operation, stability of the catalysts toward air and moisture,[38] allowing the reaction to be carried out under air atmosphere.

We believe that this novel methodology will represent a useful and efficient alternative to the traditional methods for the reduction of sulfoxides, especially, in natural products and pharmaceutical synthesis, which require mild conditions, selectivity, and functional group tolerance.

Acknowledgments

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35. In a typical experiment, to a solution of catalyst (1 mol %) and sulfoxide (1.0 mmol) in THF (3 ml) was added $PhSiH_3$ (1.0 mmol). The reaction mixture was stirred at room temperature under air atmosphere 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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38. Oxo-rhenium complexes $ReIO_2(PPh_3)_2$, $ReOCl_3(PPh_3)_2$, Re_2O_7, MTO, and $ReOCl_3$(dppm) are commercially available compounds.