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Reduction of aldehydes catalyzed by oxo-rhenium(V) complexes containing heterocyclic ligands

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ABSTRACT

This work describes the catalytic activity of several oxo-rhenium complexes containing the heterocyclic ligands 2-(2-hydroxy-5-methylphenyl)benzotriazole (Hhmpbta), 2-(2-hydroxyphenyl)benzothiazole (Hhpbt), 2-(2-hydroxyphenyl)benzoxazole (Hhpbo), 2-(2-hydroxyphenyl)-1*H*-benzimidazole (Hhpbi), isoquinoline-1-carboxylic acid (iqcH), and 4-methoxy-2-quinolinecarboxylic acid (mqcH) in the reduction of 4-nitrobenzaldehyde using phenylsilane as reducing agent. In general, all of the catalysts tested gave good to excellent yields of the 4-nitrobenzyl alcohol. Although, the best result was obtained with the catalytic system $PhSiH_3$/[$ReOBr_2$(hmpbta)(PPh_3)] (5 mol %). This system was also applied to the reduction of a large variety of aldehydes, producing the corresponding primary alcohols in good to excellent yields and good chemoselectivity.

The selective reduction of carbonyl groups is an important transformation in chemistry and represents a challenge in both chemical and pharmaceutical industries. In particular, benzylic alcohols occupy an important position in organic synthesis as target molecules of biological interest and synthetic intermediates. For these reasons, the development of new methodologies for the chemoselective reduction of carbonyl groups remains a challenge in organic synthesis.

In 2003 Toste and co-workers have demonstrated that the high valent oxo-rhenium complex $ReIO_2(PPh_3)_2$ was an excellent catalyst for the hydrosilylation of aldehydes and ketones to the corresponding silyl ethers using silanes as reducing agents.[1] Since then, several studies were reported in the literature for the hydrosilylation and for the reduction of the carbonyl group to the corresponding alcohols catalyzed by several oxo-rhenium and oxo-molybdenum complexes.[2–9]

In our previous works, we have demonstrated that several oxo-rhenium complexes containing the heterocyclic ligands Hhmpbta, Hhpbt, Hhpbo, and Hhpbi were excellent catalysts for the direct reductive amination of aldehydes, producing secondary and tertiary amines in good to excellent yields[10] and also for the deoxygenation of a large variety of sulfoxides using silanes and boranes as reducing agents.[11]

In continuation of our studies on the use of oxo-molybdenum and oxo-rhenium complexes as excellent catalysts for organic reductions,[12] in this work we explore the catalytic activity of several oxo-rhenium complexes with general formula [$ReOX_2$(L)(PPh_3)](X = Cl, Br), containing different heterocyclic ligands (Fig. 1), namely, 2-(2-hydroxy-5-methylphenyl)benzotriazole (Hhmpbta),[13] 2-(2-hydroxyphenyl)benzothiazole (Hhpbt),[14] 2-(2-hydroxyphenyl)benzoxazole (Hhpbo),[15] and 2-(2-hy-droxyphenyl)-1*H*-benzimidazole (Hhpbi),[16] isoquinoline-1-carboxylic acid (iqcH),[17] and 4-methoxy-2-quinolinecarboxylic acid (mqcH)[17] in the reduction of carbonyl compounds using silanes as reducing agents.

To compare the catalytic activity of these oxo-rhenium complexes, the reduction of the test substrate 4-nitrobenzaldehyde was performed with $PhSiH_3$ (2 mmol) in reflux of THF under air atmosphere, followed by deprotection of the resulting silyl ether with TBAF, affording the 4-nitrobenzyl alcohol (Table 1). In general, all of the oxo-rhenium complexes tested were efficient and produced good to excellent yields of 4-nitrobenzyl alcohol. Nevertheless, the catalysts containing the ligand Hhmpbta were the most efficient (Table 1, entries 1 and 5).

The best result was obtained with the catalyst [$ReOBr_2$(hmpbta)(PPh_3)] (5 mol %), affording the 4-nitrobenzyl alcohol after 13 min in 93% yield at reflux of THF (Table 1, entry 1). Similar reduction performed at room temperature produced the alcohol in 78% yield after 24 h (Table 1, entry 2). Using only 3 mol % or 2 mol % of this oxo-rhenium complex, the 4-nitrobenzyl alcohol was obtained in 78% and 76% yields, respectively (Table 1, entries 3- and 4). The reduction carried out in the presence of [$ReOCl_2$(hmpbta)(PPh_3)] (5 mol %) also gave the alcohol in excellent yields (91%) after 1 h

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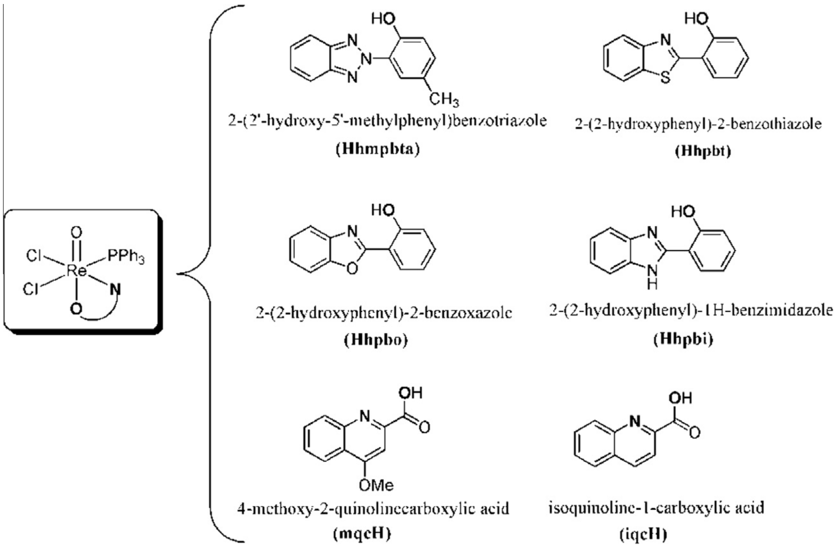
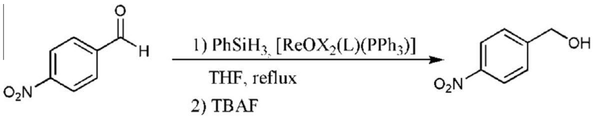
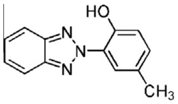
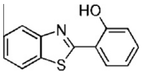
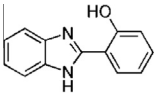
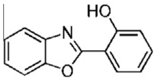
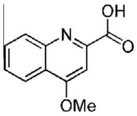
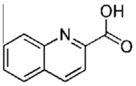


Figure 1. Structures of oxo-rhenium complexes and ligands O–N.

Table 1

Reduction of 4-nitrobenzaldehyde with $PhSiH_3$ catalyzed by oxo-rhenium complexes with the general formula $[ReOX_2(L)(PPh_3)]$($X = Cl, Br$)[a]



Entry	Catalyst	Ligand		Temp (°C)	Time	Yield (%)[b]
1	$[ReOBr_2(L)(PPh_3)]$	 **Hhmpbta**	5	Reflux	13 min	93
2	$[ReOBr_2(L)(PPh_3)]$		5	rt	24 h	78
3	$[ReOBr_2(L)(PPh_3)]$		3	Reflux	20 min	78
4	$[ReOBr_2(L)(PPh_3)]$		2	Reflux	30 min	76
5	$[ReOCl_2(L)(PPh_3)]$		5	Reflux	1 h	91
6	$[ReOBr_2(L)(PPh_3)]$	 **Hhpbt**	5	Reflux	2 h	79
7	$[ReOCl_2(L)(PPh_3)]$		5	Reflux	1 h	84
8	$[ReOCl_2(L)(PPh_3)]$	 **Hhpbi**	5	Reflux	2 h 30 min	81
9	$[ReOBr_2(L)(PPh_3)]$	 **Hhpbo**	5	Reflux	30 min	80
10	$[ReOCl_2(L)(PPh_3)]$	 **mqcH**	5	Reflux	1 h 20 min	79
11	$[ReOCl_2(L)(PPh_3)]$	 **iqcH**	5	Reflux	1 h 15 min	77
12	Without catalyst	–	–	Reflux	24 h	No reaction

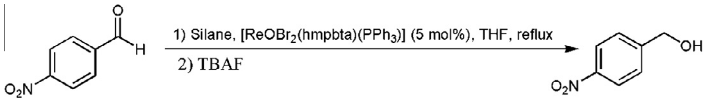
[a] The reactions were carried out with 1.0 mmol of aldehyde, 2.0 mmol of $PhSiH_3$, and 1.0 mmol of TBAF.

[b] Isolated yields.

(Table 1, entry 5). Finally, no reaction was observed in the absence of catalyst after 24 h (Table 1, entry 12).

The reduction of 4-nitrobenzaldehyde was investigated with different silanes as reducing agents catalyzed by $[ReOBr_2(hmpbta)(PPh_3)]$ (5 mol %). The best result was obtained with 2 mmol of $PhSiH_3$ at reflux temperature of THF, affording the 4-nitrobenzyl alcohol in 93% yield after 13 min (Table 2, entry 1). Similar reaction performed at room temperature produced the alcohol in 78% yield

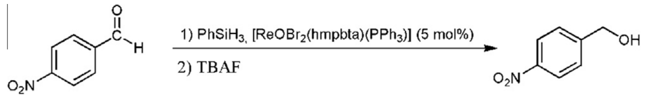
Table 2
Reduction of 4-nitrobenzaldehyde catalyzed by [ReOBr$_2$(hmpbta)(PPh$_3$)] using silanes as reducing agent[a]



Entry	Silane	Silane (mmol)	Temp	Time	Yield[b] (%)
1	$PhSiH_3$	2.0	Reflux	13 min	93
2	$PhSiH_3$	2.0	rt	24 h	78
3	$PhSiH_3$	1.2	Reflux	45 min	79
4	$PhMe_2SiH$	2.0	Reflux	5 h	69
5	$PhMe_2SiH$	3.0	Reflux	30 min	79
6	Et_3SiH	2.0	Reflux	24 h	47
7	Et_3SiH	3.0	Reflux	24 h	64
8	Ph_3SiH	3.0	Reflux	24 h	25
9	—	—	Reflux	24 h	No reaction

[a] The reactions were carried out with 1.0 mmol of aldehyde, 5 mol % of [ReOBr$_2$(hmpbta)(PPh$_3$)], and 1.0 mmol of TBAF.
[b] Isolated yields.

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



Entry	Solvent	Temp (°C)	Time	Yield[b] (%)
1	THF	66	13 min	93
2	THF	rt	24 h	78
3	CH_2Cl_2	66	13 min	79
4	CH_3CN	66	13 min	72
5	Toluene	66	13 min	61
6	Benzene	66	13 min	49
7	$CHCl_3$	66	13 min	49
8	Toluene	110	20 min	89
9	$CHCl_3$	61	3 h	88
10	CH_3CN	82	4 h	86
11	CH_2Cl_2	40	17 h	90

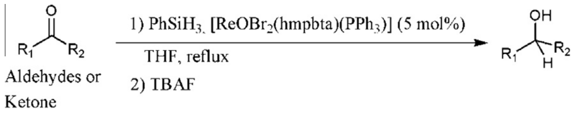
[a] The reactions were carried out with 1.0 mmol of aldehyde, 2.0 mmol of PhSiH$_3$, 5 mol % of [ReOBr$_2$(hmpbta)(PPh$_3$)], and 1.0 mmol of TBAF.
[b] Isolated yields.

after 24 h (Table 2, entry 2). The reaction carried out with 1.2 mmol of PhSiH$_3$ only gave the 4-nitrobenzyl alcohol in 79% yield (Table 2, entry 3).

The reduction performed with 2 mmol of PhMe$_2$SiH was incomplete affording only 69% yield of the alcohol (Table 2, entry 4), but using 3 mmol of PhMe$_2$SiH, this reduction required only 30 min and produced the alcohol in 79% yield (Table 2, entry 5). The reaction of 4-nitrobenzaldehyde with 2 mmol of Et$_3$SiH was also incomplete, giving the alcohol in 47% yield (Table 2, entry 6), although adding 3 mmol of Et$_3$SiH, the alcohol was isolated in 64% yield after 24 h (Table 2, entry 7). Very low yield of 4-nitrobenzyl alcohol was isolated in the reduction carried out with Ph$_3$SiH (Table 2, entries 8). Finally, no reaction was observed in the absence of silane (Table 2, entry 9).

The influence of the solvent on the reduction of 4-nitrobenzaldehyde catalyzed by 5 mol % of [ReOBr$_2$(hmpbta)(PPh$_3$)] with phenylsilane was also explored (Table 3). All the solvents tested produce good to excellent yields of 4-nitrobenzyl alcohol at reflux temperature (Table 3, entries 1, 8–11). The results obtained

Table 4
Reduction of carbonyl compounds with the catalytic system PhSiH$_3$/[ReOBr$_2$(hmpbta)(PPh$_3$)][a]



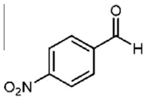
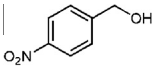
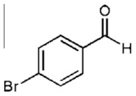
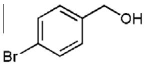
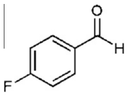
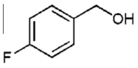
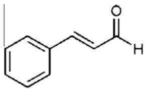
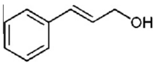
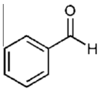
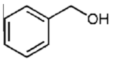
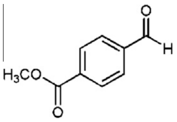
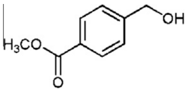
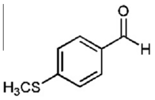
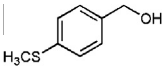
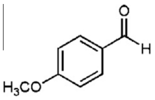
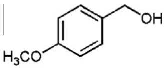
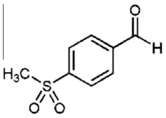
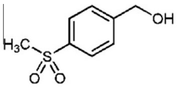
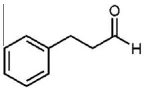
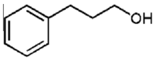
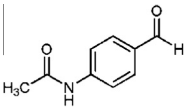
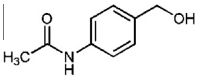
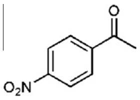
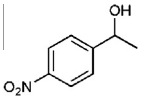
Entry	Carbonyl compound	Alcohol	Time	Yield[b] (%)
1			13 min	93
2			15 min	91
3			15 min	89
4			25 min	89

Table 4 (*continued*)

Entry	Carbonyl compound	Alcohol	Time	Yield[b] (%)
5			15 min	88
6			20 min	87
7			25 min	85
8			30 min	76
9			16 min	72
10			1 h	67
11			1 h 20 min	61
12			24 h	52

[a] The reactions were carried out with 1.0 mmol of carbonyl compound, 2.0 mmol of $PhSiH_3$, 5 mol % of $[ReOBr_2(hmpbta)(PPh_3)]$, and 1.0 mmol of TBAF.
[b] Isolated yields.

demonstrated that THF was the best solvent, affording the alcohol in 93% yield after only 13 min (Table 3, entry 1). At room temperature, the alcohol was isolated in 78% yield, but the reaction needs 24 h (Table 3, entry 2). Toluene, chloroform, acetonitrile, and dichloromethane also gave good yields of the alcohol at reflux temperature, but these reductions required more time (20 min–17 h) (Table 3, entries 8–11). We have also performed the reduction of 4-nitrobenzaldehyde catalyzed by 5 mol % of $[ReOBr_2(hmpbta)(PPh_3)]$ with phenylsilane at the same reaction temperature (66 °C) with the same reaction time (13 min) in order to compare the influence of the solvent under the same reaction conditions (Table 3, entries 1, 3–7). THF proved to be the best solvent, affording the alcohol in 93% yield (Table 3, entry 1). At 66 °C, dichloromethane and acetonitrile (Table 3, entries 3–4) also gave good yields, but toluene, benzene, and chloroform produced moderate to low yields of the alcohol (Table 4, entries 5–7).

The catalytic system $PhSiH_3/[ReOBr_2(hmpbta)(PPh_3)]$ (5 mol %) was explored in the reduction of a large variety of aldehydes in reflux of THF under air atmosphere (Table 4).[18] The reduction of the aldehydes was very fast (13 min–1 h 20 min), producing the corresponding primary alcohols in good to excellent yields. This method proved to be highly chemoselective, tolerating a large range of functional groups, such as $-NO_2$, $-SO_2R$, $-CO_2R$, –NHCOR, –F, –Br, $-OCH_3$, $-SCH_3$, and double bond.

This catalytic system was also tested in the reduction of 4-nitroacetophenone, but only produced the corresponding secondary alcohol in moderate yields (52%) after 24 h (Table 4, entry 12).

In conclusion, we have studied the catalytic activity of several oxo-rhenium complexes containing the heterocyclic ligands Hhmpbta, Hhpbt, Hhpbo, Hhpbi, mqcH, and iqcH as catalysts in the reduction of substrate test 4-nitrobenzaldehyde using phenylsilane as reducing agent. All the catalysts tested show good to excellent catalytic activities. The best results were obtained with the catalytic system $PhSiH_3/[ReOBr_2(hmpbta)(PPh_3)]$ (5 mol %) in reflux of THF under air atmosphere. This catalytic system was also very efficient for the reduction of a large variety of aldehydes in good to excellent yields with high chemoselectivity, tolerating a large range of functional groups, such as $-NO_2$, $-SO_2R$, $-CO_2R$, –NHCOR, –F, –Br, –OMe, –SMe, and double bond. However, moderate yields were obtained in the reduction of 4-nitroacetophenone.

The reductions of the aldehydes were very fast and the catalysts are stable toward air and moisture, which allows the reactions to be performed under air. We believe that this new method can be a useful alternative to the other methods described in the literature for the reduction of aldehydes.

Further studies to explore the catalytic activity of other oxo-rhenium complexes as well as to extend this methodology to the reduction of other substrates are now under investigation in our group.

Acknowledgments

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18. In a typical experiment, to a mixture of carbonyl compound (1.0 mmol) and [$ReOBr_2$(hmpbta)(PPh_3)] (5 mol %) in THF (3 mL) at reflux temperature was added $PhSiH_3$ (2.0 mmol). The reaction mixture was stirred under air atmosphere (the reaction times are indicated in the Table 4) and the progress of the reaction was monitored by TLC or ^{1}H NMR. Upon completion, the reaction was quenched with 1 equiv of tetrabutylammonium fluoride (TBAF) (1.0 M THF) during 1 h. Then, 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 alcohols, which are all known compounds.