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Cyclopentadienyl-ruthenium(II) complexes as efficient catalysts for the reduction of carbonyl compounds

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ABSTRACT

This work reports the reduction of a large variety of aldehydes and ketones with the system $PhSiH_3$/$[CpRu(PPh_3)_2Cl]$ in good to excellent yields and high chemoselectivity. The catalyst $[CpRu(PPh_3)_2Cl]$ can be used in at least 12 catalytic cycles with excellent catalytic activity and several substrates were reduced under solvent free conditions.

1. Introduction

Alcohols are important building blocks for the synthesis of a number of pharmaceuticals, agrochemicals and fine chemicals. The reduction of carbonyl compounds to yield primary and secondary alcohols is a very desirable reaction, since carbonyl compounds are among the most abundant starting materials for the synthetic chemist. Therefore, the development of new methodologies for the chemoselective reduction of carbonyl groups remains a challenge in organic synthesis.

Among the large variety of catalysts reported in the literature for the reduction of carbonyl compounds, the use of ruthenium complexes has received significant attention. For example, several ruthenium complexes have been employed as catalysts for the hydrogenation of carbonyl compounds, providing an efficient access to the corresponding alcohols.[1–4]

Transfer hydrogenation of carbonyl compounds catalyzed by ruthenium complexes with 2-propanol is convenient in large scale synthesis since there is no need to employ a high hydrogen pressure or to use hazardous reducing agents.[5–8]

The hydrosilylation is also an important methodology for the reduction of carbonyl compounds, producing initially a silyl ether which can easily be hydrolyzed to the corresponding alcohol. Due to its safety and operational simplicity, the catalytic hydrosilylation of carbonyl compounds has recently become an important alternative as a reduction strategy. In contrast to the other reduction methodologies, ruthenium complexes have not been widely used as catalysts in the hydrosilylation of carbonyl compounds.[9–12]

Cyclopentadienyl-ruthenium(II) complexes have been the subject of investigation by many research groups during past couple of decades not only because of their potential as catalysts[13–16] but also due to their strong anticancer activity.[17–20]

In continuation of our work about the hydrosilylation of carbonyl compounds catalyzed by molybdenum[21,22] and rhenium[23] complexes, here we report a novel methodology for the efficient reduction of aldehydes and ketones with silanes catalyzed by cyclopentadienyl ruthenium (II) complexes.

2. Results and discussion

The reduction of the test substrate 4-(methylthio)benzaldehyde was investigated with different CpRu(II) complexes, silanes and solvents. Initially, the reduction of 4-(methylthio)benzaldehyde was explored with different CpRu(II) complexes (1 mol%) (Fig. 1) with phenylsilane at 80 °C under solvent free conditions. All catalysts afforded the alcohol as the major product and the silyl ether as the minor one in 20–35% yields. After hydrolysis of the silyl ether with tetrabutylammonium fluoride (TBAF), 4-(methylthio)benzyl

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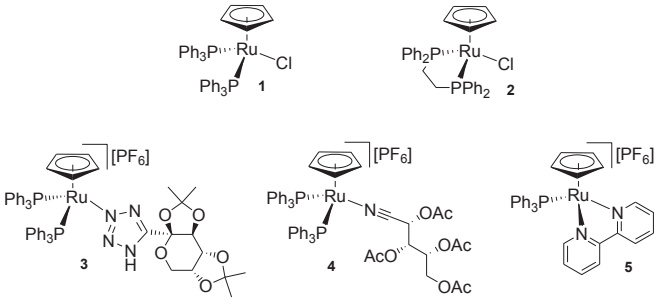


Fig. 1. Structures of the CpRu (II).

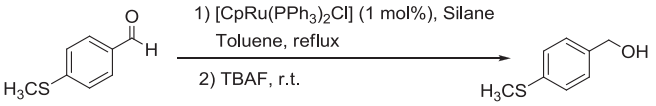
alcohol was obtained in excellent yields. The complex $[CpRu(PPh_3)_2Cl]$ **1** (1 mol%) proved to be the best catalyst for this reduction, producing the corresponding benzyl alcohol in 98% yield after 40 min (Table 1, entry 1). Using only 0.5 mol% of $[CpRu(PPh_3)_2Cl]$, the reaction also afforded the alcohol in excellent yield, but required 24 h (Table 1, entry 2). At room temperature, the product was isolated in 89% yield after 24 h (Table 1, entry 3). The ruthenium complex [CpRu(dppe)Cl] **2** required 24 h to reduce the aldehyde in 95% yield (Table 1, entry 4).

In our previous works,[17,18] we have demonstrated the excellent biological activity of cyclopentadienyl ruthenium (II) complexes **3** and **4**, containing fructose and xylose carbohydrate derivative moieties, respectively. In this work we explored the catalytic activity of these monocationic, *N*-bonded complexes in the reduction of carbonyl compounds, to study the influence of these structural changes on their catalytic activity when compared with the parent complex $[CpRu(PPh_3)_2Cl]$. The reactions catalyzed by complexes **3** and **4**, were very fast (20 min-1h), producing the alcohol in good to excellent yields (Table 1, entries 5–6). The complex $[RuCp(PPh_3)(2,2'\text{-bipy})][PF_6]$ **5** was also efficient in the reduction of the aldehyde with 84% yield after 3 h (Table 1, entry 7). Finally, in absence of catalyst was observed the formation of the alcohol in only 30% yield after 24 h (Table 1, entry 8). Complex $[CpRu(PPh_3)_2Cl]$ proved to be the most efficient catalyst for the conversion of 4-(methylthio)benzaldehyde in 4-(methylthio) benzyl alcohol, within the CpRu(II) compounds tested.

The reactivity of different silanes was also evaluated in the reduction of the 4-(methylthio)benzaldehyde catalyzed by $[CpRu(PPh_3)_2Cl]$ (1 mol%). The best result was obtained with $PhSiH_3$, affording the alcohol in 96% yield after 40 min (Table 2, entry 1). The silanes $PhMe_2SiH$, Ph_3SiH, Pr_3SiH, Et_3SiH and polymethylhydrosiloxane (PMHS) also produced good yields of 4-(methylthio)benzyl alcohol, but these reactions required 24 h (Table 2, entries 2–6). In absence of silane we did not observe the reduction of the aldehyde (Table 2, entry 7).

The reduction of 4-(methylthio)benzaldehyde catalyzed by

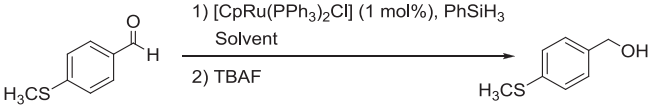
Table 2
Reduction of 4-(methylthio)benzaldehyde catalyzed by $[CpRu(PPh_3)_2Cl]$ using different silanes.[a]



Entry	Silane	Time	Yield[b]
1	$PhSiH_3$	40 min	96
2	Me_2PhSiH	24 h	87
3	Ph_3SiH	24 h	83
4	PMHS	24 h	75
5	Pr_3SiH	24 h	70
6	Et_3SiH	24 h	66
7	Without silane	24 h	No reaction

[a] The reactions were carried out with 1.0 mmol of 4-(methylthio)benzaldehyde, 1.2 mmol of silane and TBAF (1.0 mmol).
[b] Isolated yields.

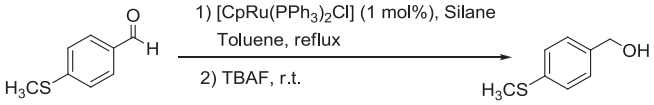
Table 3
Reduction of 4-(methylthio)benzaldehyde catalyzed by $[CpRu(PPh_3)_2Cl]$ in different solvents.[a]



Entry	Solvent	Temp. (°C)	Time	Yield (%)[b]
1	Neat	80	40 min	98%
2	Toluene	Reflux	40 min	96%
3	Toluene	r. t.	24 h	89%
4	THF	Reflux	2 h	92%
5	Benzene	Reflux	24 h	97%
6	CH_2Cl_2	Reflux	24 h	95%
7	$CHCl_3$	Reflux	24 h	94%
8	CH_3CN	Reflux	24 h	21%

[a] The reactions were carried out with 1.0 mmol of 4-(methylthio)benzaldehyde, 1.2 mmol of $PhSiH_3$ and TBAF (1.0 mmol).
[b] Isolated yields.

Table 1
Reduction of 4-(methylthio)benzaldehyde catalyzed by different CpRu(II) complexes.[a]



Entry	Catalyst	Catalyst (mol%)	Temp. (°C)	Time	Yield (%)[b]
1	$[CpRu(PPh_3)_2Cl]$ **1**	1.0	80	40 min	98
2	$[CpRu(PPh_3)_2Cl]$ **1**	0.5	80	24 h	93
3	$[CpRu(PPh_3)_2Cl]$ **1**	1.0	r.t.	24 h	89
4	[CpRu(dppe)Cl] **2**	1.0	80	24 h	95
5	$[RuCp(PPh_3)_2(TFru)][PF_6]$ **3**	1.0	80	1 h	98
6	$[RuCp(PPh_3)_2NCXylAc][PF_6]$ **4**	1.0	80	20 min	72
7	$[RuCp(PPh_3)(2,2'\text{-bipy})][PF_6]$ **5**	1.0	80	3 h	84
8	Without catalyst	–	80	24 h	30

[a] The reactions were carried out with 1.0 mmol of 4-(methylthio)benzaldehyde, 1.2 mmol of $PhSiH_3$ and 1.0 mmol TBAF.
[b] Isolated yields.