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Highly efficient aerobic oxidation of benzylic and allylic alcohols by a simple catalyst system of $[RuCl_2(p\text{-cymene})]_2/Cs_2CO_3$

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Abstract

A new catalyst system of $[RuCl_2(p\text{-cymene})]_2/Cs_2CO_3$ has been disclosed for highly efficient aerobic oxidation of activated alcohols to the corresponding carbonyl compounds, which is characterized by its high selectivity and activity, operational simplicity, and low air and moisture sensitivity.

From an economical and environmental point of view the use of molecular oxygen as a stoichiometric reoxidant has attracted considerable attention, and recently there have been great efforts in the development of efficient and selective aerobic oxidation protocols catalyzed by transition metal complexes.[1] Among the various complexes employed for the chemistry, and in particular, some ruthenium catalysts such as $RuCl_2(PPh_3)_3$[2] or $Pr_4N^+\cdot RuO_4^-$[3] in the presence of other co-catalysts or additives, have appeared to be some of the promising candidates to meet the facile green chemistry. However, despite some recent progress, there is still a need to develop a new procedure for aerobic oxidation employing a more convenient catalyst system of high activity, operational simplicity, and low air and moisture sensitivity. Here we describe our initial efforts towards this goal.

Among a variety of easily available ruthenium complexes tested as oxidation catalysts, we found that the use of $[RuCl_2(p\text{-cymene})]_2$ (**1**)[4] coupled with some additives displayed a high catalytic activity on the oxidation under atmospheric oxygen.[5]

As shown in Table 1, whereas benzyl alcohol was oxidized very slowly under the oxygen atmosphere by the ruthenium complex **1** alone, a significant rate enhancement was observed in the presence of molecular sieves under the same conditions. After extensive experiments on the effects of other additives, we discovered that cesium carbonate exhibited the most dramatic rate

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enhancement of the aerobic oxidation in combination with the ruthenium complex **1** (entry 5). We were finally pleased to observe that even a catalytic amount of the cesium salt was enough to perform the aerobic oxidation with almost the same efficiency as in the stoichiometric reaction (entry 7).[6] Whereas the reaction was most efficiently carried out in the temperature range of 90–110°C, conversion was slowed down upon reducing the temperatures. Other bases such as K_2CO_3, *t*-BuOK, $CsOH{\cdot}H_2O$, or amines were less effective compared with cesium carbonate (for example, entry 9). Cesium alkoxides are distinguished from other alkali metal counterparts in view of nakedness, weak conjugation, high solubility, appropriate basicity, good stability, and/or weak solvation.[7] The metal-catalyzed aerobic oxidation is generally known to proceed via the formation of an alkoxy metal intermediate, which subsequently undergoes β-elimination to afford carbonyl compounds and a metal hydride.[8] Although the exact role of Cs_2CO_3 in the present oxidation system awaits further studies, the cesium salt possibly facilitates the initial stage of the reaction: formation of the alkoxy ruthenium intermediate in the catalytic cycle.

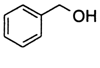
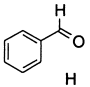
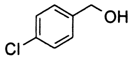
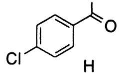
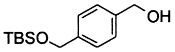
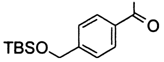
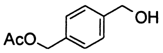
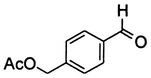
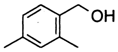
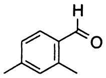
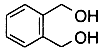
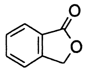
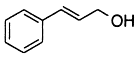
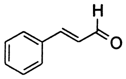
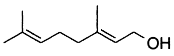
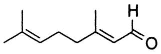
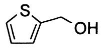
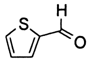
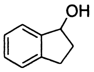
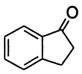
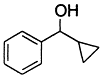
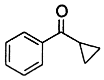
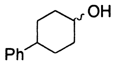
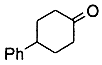
Table 1
Aerobic oxidation of benzyl alcohol to benzaldehyde catalyzed by **1**[a]

Entry	**1** (equiv.)	Additive (equiv.)	*T*/°C	*t*/h	Conversion (%)[b]
1	–	–	100	12	<5
2	0.2	–	100	12	25
3	0.2	MS 4 Å[c]	100	12	80
4	–	MS 4 Å[c]	100	12	<5
5	0.2	Cs_2CO_3 (1.2)	100	1.0	>99
6	–	Cs_2CO_3 (1.2)	100	12	<5
7	**0.03**	**Cs_2CO_3 (0.1)**	**100**	**2.5**	**>99**
8	0.03	Cs_2CO_3 (0.1)	50	12	77
9	0.03	K_2CO_3 (0.1)	100	12	68

[a] All reactions were performed under O_2 atmosphere (using an O_2 balloon) and in 0.6 M concentration.
[b] Conversion was determined by ^1H NMR of the crude reaction mixture.
[c] Used in 0.4 g/mmol of the alcohol.

Under the explored standard conditions, a range of alcohols were evaluated as substrates for the aerobic oxidation (Table 2).[9] All the tested primary alcohols of benzylic and allylic position were smoothly and quantitatively converted into the corresponding aldehydes in excellent yields (entries 1–9). Electronic and/or steric variation of the alcohols has little effect on the efficiency of the aerobic oxidation. Common protecting groups such as silylether or acetate were tolerant under the present protocol (entries 3 and 4). It is especially noteworthy that a nearby diol such as 1,2-benzenedimethanol was oxidized in excellent yield to afford the corresponding lactone (entry 6). Allylic alcohols were also good substrates, and in this case no isomerization of the conjugated double bonds was observed (entries 7 and 8). Heteroatoms such as sulfur did not result in any notorious effects on the catalytic system (entry 9). Aromatic ketones were produced in an equally efficient way by the aerobic oxidation from the corresponding secondary alcohols (entries 10 and 11). Whereas benzylic and allylic alcohols were oxidized in a highly efficient way, aliphatic alcohols were less reactive under the conditions established here and therefore higher loading of the catalyst **1** and Cs_2CO_3 was required to obtain the aliphatic carbonyl compounds in good yields (entry 12). It should also be noted that under the present catalytic oxidation

Table 2
Aerobic oxidation of various alcohols by a catalyst system of $[RuCl_2(p\text{-cymene})]_2$ (**1**, 5 mol%)/Cs_2CO_3 (10 mol%)[a]

Entry	Alcohol	*t*/h	Product	Isolated yield
1		1		91
2		1		94
3		1		99
4		1		87
5		1		98
6		2		95
7		1		85
8		3		95
9		2		94
10		3		81
11		5		94
12[b]		5		83

[a] All reactions were carried out at 100°C in toluene (0.6 M) under an oxygen atmosphere (using an O_2 balloon).
[b] In this case, 15 mol% of **1** was used in combination with 1.0 equiv. of Cs_2CO_3.

system, selectivity for the corresponding aldehyde or ketones was >99% in all cases and no other over-oxidized compounds were detected.

In summary, catalytic amounts of cesium carbonate have profound effects on the $[RuCl_2(p\text{-cymene})]_2$ catalyzed aerobic oxidation and a variety of benzylic and allylic alcohols were aerobically oxidized in excellent yields using the catalyst system. Aliphatic substrates, however, were less effective and further studies concerning this aspect is currently underway.

Acknowledgements

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6. Although reaction time was longer (6 h), smaller amounts (5 mol%) of Cs_2CO_3 could also be used to result in a complete conversion with the use of 3 mol% of **1** under the same reaction conditions.
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9. Representative experimental procedure: To a solution of 4-chlorobenzyl alcohol (285 mg, 2.0 mmol) in toluene (3.3 mL) was added Cs_2CO_3 (65 mg, 0.2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (61 mg, 0.1 mmol) and the reaction mixture was stirred for 1 h at 100°C under an oxygen atmosphere (using an O_2 balloon). After cooling to room temperature, hexane (10 mL) was added and the mixture was filtered on celite, washing with hexane. Purity of the crude reaction mixture was determined to be >95% by ^1H NMR integration after removal of the solvent. Column chromatography on silica gel (ethyl acetate/hexane = 1/3) provided the analytically pure product, 4-chlorobenzaldehyde (264 mg, 94%).