

## Ruthenium-catalysed Oxidation of Alcohols by Acetone

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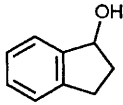
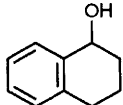
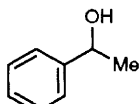
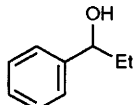
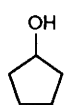
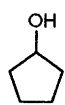
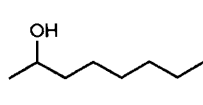
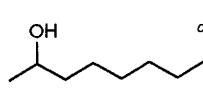
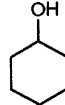
Secondary alcohols are readily converted to ketones under mild conditions by acetone in the presence of a catalytic amount of  $\text{RuCl}_2(\text{PPh}_3)_3$ ; in some cases the reaction is co-catalysed by acetophenone.

Oxidation of alcohols to aldehydes and ketones is of great importance in organic synthesis.<sup>1-3</sup> Transition metal-catalysed oxidations have recently attracted considerable interest and a number of oxidants and transition metals have been explored in order to develop methods for mild and selective oxidation of alcohols. Some success using ruthenium catalysts<sup>4-7</sup> has been achieved with *tert*-butyl hydroperoxide,<sup>4</sup> chloramine-T,<sup>4</sup>

*N*-methyl morpholine oxide,<sup>4</sup> benzoquinone,<sup>5</sup> molecular oxygen,<sup>5,6</sup> iodosylbenzene<sup>7</sup> and  $\text{NaIO}_4$ .<sup>8</sup> Recently we reported a mild procedure for the ruthenium-catalysed aerobic oxidation of alcohols,<sup>5</sup> and in related work we described a mild ruthenium-catalysed transfer hydrogenation by propan-2-ol in the presence of base.<sup>9</sup>

The procedure reported here employs ruthenium com-

**Table 1** RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>-Catalysed oxidation of secondary alcohols to ketones by an excess of acetone<sup>a</sup>

Entry	Substrate	Conversion to ketone (%) <sup>b</sup>	Isolated yield of ketone (%)	Time/h
1		93.7		0.5
		97.5	90.8	1.0
2		64.1		2.0
		98.5	89.5	7.0
3		89.2		1.0
		97.1	85.7	2.0
4		52.6		2.0
		85.7	80.2	12
5		28.7		0.5
		94.1		1.5
6		49.0		0.5
		94.3		1.0
7		9.55		4.0
		27.4		40
8		32.6		4.0
		60.4		12
9		20.7		4.0
		61.5		12

<sup>a</sup> The reaction was performed on a 10 mmol scale in 10 ml of acetone with a substrate to catalyst ratio of 1000:1. <sup>b</sup> Determined by gas chromatography. The selectivity for ketones was more than 99%. <sup>c</sup> 82 mg (0.68 mmol) of acetophenone was added.

plexes as catalyst and acetone as hydrogen acceptor which is inexpensive and unreactive towards most organic functional groups. In the presence of base (K<sub>2</sub>CO<sub>3</sub>), secondary alcohols were catalytically converted to the corresponding ketones at 56 °C. This procedure is superior to the classical Oppenauer oxidation for which a stoichiometric amount of aluminum *tert*-butoxide is required.<sup>3</sup> Several ruthenium complexes, such as RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>, RuCl<sub>2</sub>(dmsO)<sub>4</sub>-PPh<sub>3</sub> (dmsO = dimethyl sulfoxide) and RuCl<sub>2</sub>(dmsO)<sub>4</sub>-2PPh<sub>3</sub> were tried as catalyst precursors and in all cases K<sub>2</sub>CO<sub>3</sub> was employed as base. Some results using RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> are listed in Table 1.†

† The reactions were generally performed on a 10 mmol scale under N<sub>2</sub> atmosphere. A substrate to catalyst ratio of 1000:1 was used, although in some cases, *e.g.*, entry 1, a ratio of 5000:1 could be used. 10 ml acetone was employed both as hydrogen acceptor and as solvent, and 138 mg (1 mmol) K<sub>2</sub>CO<sub>3</sub> was used to provide a basic medium. The conversions were determined by GC and some of the products were isolated by silica gel column chromatography.

**Table 2** Effect of the ruthenium complexes on the oxidation of 1-phenylethanol to acetophenone<sup>a</sup>

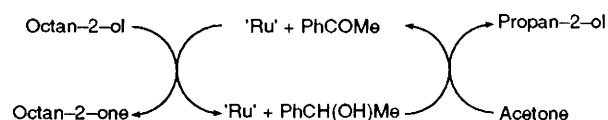
Catalyst precursor	Conversion to ketone (%) <sup>b</sup>	Time/h
RuCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>3</sub>	97.1	2.0
RuCl <sub>2</sub> (dmsO) <sub>4</sub> + PPh <sub>3</sub>	27.1	2.0
	84.2	16
RuCl <sub>2</sub> (dmsO) <sub>4</sub> + 2PPh <sub>3</sub>	8.40	1.5
	45.9	20

<sup>a</sup> The reaction was performed on a 10 mmol scale in 10 ml of acetone with a substrate to catalyst ratio of 1000:1. <sup>b</sup> Determined by gas chromatography. The selectivity for ketones was more than 99%.

**Table 3** RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>-Catalysed oxidation of PhCH(OH)(Me) and octan-2-ol in a 1:1 mixture<sup>a</sup>

Time/h	Conversion to ketones (%) <sup>b</sup>	
	PhCH(OH)Me	Octan-2-ol
2.0	48.0	18.2
4.5	62.7	29.4
20	86.4	54.7
40	89.8	61.8

<sup>a</sup> The reaction was performed on a 20 mmol scale in 20 ml acetone with substrate to catalyst ratio of 2000:1. <sup>b</sup> Determined by gas chromatography.

**Scheme 1** Postulated catalytic cycle for the oxidation of octan-2-ol in the presence of acetophenone

Examination of Table 1 reveals that (i) alcohols bearing an aromatic ring at the  $\alpha$ -position generally give more satisfactory results than simple aliphatic alcohols, both with respect to conversion and reaction rate, and (ii) alcohols of five-membered rings were more reactive than those of six-membered rings and acyclic substrates. Indan-1-ol was the most reactive substrate of those studied, and its oxidation was complete within 30 min, corresponding to 1900 turnovers h<sup>-1</sup>.

The combination of RuCl<sub>2</sub>(dmsO)<sub>4</sub><sup>10</sup> and one or two equivalents of triphenylphosphine also catalysed the oxidation of secondary alcohols to ketones, but the reaction rate was lower. The outcome of the oxidation of 1-phenylethanol using different ruthenium catalysts is shown in Table 2.

In this oxidation process, a catalytic amount of base such as K<sub>2</sub>CO<sub>3</sub> is necessary. Practically, however, an excess of K<sub>2</sub>CO<sub>3</sub> (1 mmol) was used, so that water from substrates could also be removed.

Unfortunately, all these systems failed to catalyse the oxidation of primary alcohols to the corresponding aldehydes. This is probably owing to the formation of inactive ruthenium hydridocarbonyl or carbonyl complexes. It is well known that base promotes the reaction of ruthenium chloride-tertiary phosphine complexes with primary alcohols resulting in the formation of stable hydridocarbonyl or carbonyl complexes of ruthenium.<sup>11,12</sup>

As shown in Table 1 (entries 3 and 7) the rate of oxidation of 1-phenylethanol to acetophenone is at least 30 times faster than that of octan-2-ol. Surprisingly, the oxidation of a 1:1 mixture of these alcohols did not show the expected selectivity (Table 3). Thus, after 2 h the ratio of acetophenone to octan-2-one was 2.6:1. From the results in Table 3 it is evident that the reaction rate for oxidation of octan-2-ol has signifi-

cantly increased compared to its oxidation in the absence of acetophenone. This observation suggests that the active species generated by acetophenone/1-phenylethanol promotes the oxidation of octan-2-ol. Furthermore, it was found that a catalytic amount of acetophenone was enough to accelerate the oxidation of octan-2-ol to octan-2-one by a factor of 10. Thus, in the presence of a catalytic amount of acetophenone, 60.2% conversion of octan-2-ol could be achieved in 12 h, while without acetophenone the reaction gave only 27.4% conversion in 40 h (entries 7 and 8 in Table 1). The same effect was also observed when 1-phenylethanol was used in place of acetophenone. However, the very reactive indan-1-ol does not have such an effect. The role of acetophenone or 1-phenylethanol is currently under investigation, and a catalytic cycle is tentatively formulated in Scheme 1.

In the present work, we have succeeded in carrying out a ruthenium-catalysed dehydrogenation of alcohols under very mild reaction conditions, and a remarkable catalytic effect by acetophenone was observed.

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