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Aerobic Oxidation of Alcohols with Ruthenium–Cobalt Bimetallic Catalyst in the Presence of Aldehydes

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Summary: Oxidation of alcohols can be performed highly efficiently at room temperature with molecular oxygen (1 atm) in the presence of an aldehyde and $RuCl_3$–$Co(OAc)_2$ bimetallic catalyst.

Metal-catalyzed oxidations of alcohol are of importance in synthesis and biological systems.[1] The aerobic oxidation with metal catalysts is a highly attractive method for economical and environmental reasons. However, most of the reported methods for aerobic oxidation of alcohols are applicable only to activated alcohols such as benzyl,[2] allyl,[2a,b,3] and α-keto alcohols.[4] General methods are limited to a few reactions which involve Pt-,[5] $Ru_3O(O_2CR)_6L_3^+$-,[6] and $PdCl_2$–NaOAc-catalyzed reactions,[7] and these require rather high reaction temperature, high pressure of O_2, or long reaction times.

Recently, we found that a low-valent ruthenium catalyst/peroxide system is effective for the specific oxidations of various substrates such as amines,[8] amides,[9] nitriles,[10] and hydrocarbons.[11] The catalytically active species of these reactions seems to be a low-valent oxoruthenium complex.[12] Further study revealed that the oxoruthenium species can be generated by the reaction of low valent ruthenium complexes with molecular oxygen in the presence of aldehydes and that the oxygenations of β-lactams[13] and alkanes[14] with molecular oxygen can be also performed efficiently at room temperature in the presence of aldehydes. Considering the high reactivity of oxoruthenium complexes toward alcohols,[15,16] the aerobic oxidation of alcohols in the presence of aldehydes under mild conditions seemed feasible. However, under these conditions, the oxidation does not occur because the formation of peracids[12] is prevented by strong coordination of alcohol to the ruthenium. Therefore, we examined catalysts which are known to efficiently form peracids from aldehydes and molecular oxygen[17] and have no strong coordination ability toward alcohols. We have now found a novel, general, and efficient method for the aerobic oxidation of alcohols by using a ruthenium–cobalt bimetallic catalyst. The oxidation of alcohols is performed at room temperature with molecular oxygen (1 atm) in the presence of an aldehyde and $RuCl_3$–$Co(OAc)_2$ bimetallic catalyst (eq 1). This method is particularly convenient

$$R^1CH(OH)R^2 \xrightarrow[O_2,\ RCHO]{RuCl_3\text{–}Co(OAc)_2\ (cat.)} R^1C(O)R^2 \qquad (1)$$

because of simple operation, mild reaction conditions, and high efficiency.

The catalytic activity of various transition metal complexes was examined as follows: A mixture of 4-octanol (**1**, 2.00 mmol), acetaldehyde (2.00 mmol), and a catalyst (0.02 mmol) in ethyl acetate (12 mL) was stirred at room temperature for 1 h under an oxygen atmosphere (1 atm, balloon). Unsatisfactory results were obtained by using metal complex catalysts such as $RuCl_3{\cdot}nH_2O$ (conversion of **1**, 8%; yield of 4-octanone (**2**), 0%), $RuCl_2(PPh_3)_3$ (0%; 0%), 5% Ru/C (0%; 0%), $Ni(acac)_2$ (1%; 88%), $Cu(OAc)_2$ (15%; 87%), $CuCl_2$ (6%; 17%), $MnCl_2$ (4%; 25%), and $Co(OAc)_2{\cdot}4H_2O$ (25%; 87%). However, ketone **2** was obtained efficiently (76%; 93%) when a 1:1 mixture of $RuCl_3{\cdot}nH_2O$ and $Co(OAc)_2{\cdot}4H_2O$ was used as a catalyst. Ethyl acetate proved to be a good solvent; however, nonpolar solvents such as benzene, hexane, and dichloromethane retarded the reaction. The effect of the aldehyde was examined for the aerobic oxidation of **1** in the presence of the Ru–Co catalyst. Various aliphatic aldehydes such as acetaldehyde (76%; 93%), heptanal (71%; 81%), 2,2-dimethylpropanal (55%; 99%), and cyclohexanecarboxaldehyde (58%, 99%) gave satisfactory results, but the reaction proceeded slowly in the presence of benzaldehyde (33%; 91%). The use of acetaldehyde is practical because of its efficiency, low cost, and easy separation of acetic acid formed from the reaction mixture.

A typical experimental procedure is exemplified by the oxidation of L-menthol (**3**). To a stirred mixture of L-menthol (1.56 g, 10.0 mmol), $RuCl_3{\cdot}nH_2O$ (0.026 g, 0.10 mmol), and $Co(OAc)_2{\cdot}4H_2O$ (0.025 g, 0.10 mmol) in ethyl acetate (50 mL) was added a solution of acetaldehyde (1.76

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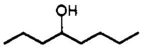
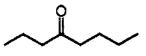
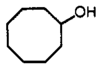
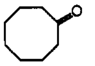
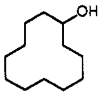
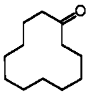
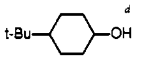
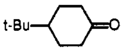
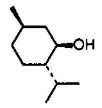
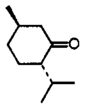
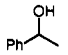
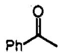
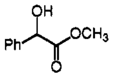
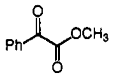
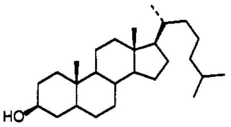
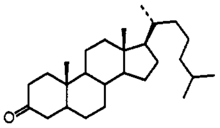
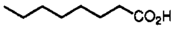
Table I. Aerobic Oxidation of Alcohols with Ruthenium-Cobalt Bimetallic Catalyst in the Presence of Acetaldehyde[a]

entry	alcohol	product[b]	yield,[c] %
1	 1	 2	89
2			95
3			97
4	 [d]		91
5	 3	 4	95
6			94
7			78
8			98
9			96

[a] All reactions were carried out according to the procedure described in the text. [b] Satisfactory IR, NMR and mass spectral data were obtained. [c] Isolated yield based on the starting alcohol. [d] *Cis/trans* = 1/2.

g, 40.0 mmol) in ethyl acetate (10 mL) dropwise at 20 °C over a period of 1.5 h under an oxygen atmosphere (1 atm, balloon). After being stirred for an additional 1.5 h, the reaction mixture was quenched by pouring into aqueous 1 M Na_2SO_3 solution (10 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 40 mL). The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution (45 mL) and brine (30 mL), and dried over $MgSO_4$. Removal of the solvent under reduced pressure gave L-menthone (4, 1.47 g, 95%, $[\alpha]^{25}_D$ −29.6° (neat) (lit.[18] $[\alpha]_D$ −29.6° (neat))).

Representative results of the aerobic oxidation of alcohols are summarized in Table I. Various aliphatic and aromatic secondary alcohols can be oxidized at room temperature under an O_2 atmosphere (1 atm). Because most of the reactions proceed quantitatively, the products can be readily isolated only by removal of acetic acid and the catalyst through washing. Methyl mandelate undergoes oxidation to the corresponding 1,2-dicarbonyl compounds (entry 7). Primary alcohols are oxidized smoothly to the corresponding carboxylic acids (entry 9).

The present aerobic oxidation can be rationalized by assuming the following two sequential pathways: (i) formation of peracids by a cobalt-mediated radical chain reaction of aldehydes with molecular oxygen[17] and (ii) ruthenium-catalyzed oxidation of alcohols[15] with the peracids thus formed. Thus, the reaction of an aldehyde

$$\mathrm{RCHO} + \mathrm{Co(III)} \rightarrow \underset{\mathbf{5}}{\mathrm{RCO^{\bullet}}} + \mathrm{Co(II)} + \mathrm{H^+}$$

$$\mathbf{5} + \mathrm{O_2} \rightarrow \underset{\mathbf{6}}{\mathrm{RC(O)OO^{\bullet}}}$$

$$\mathbf{6} + \mathrm{RCHO} \rightarrow \underset{\mathbf{7}}{\mathrm{RC(O)OOH}} + \mathbf{5}$$

with the cobalt(III) complex derived from a Co(II) complex[17a] gives the acyl radical **5**, which reacts with molecular oxygen to afford the acylperoxy radical **6**. The radical **6** abstracts hydrogen from the aldehyde to give peracid **7** and the radical **5**. Reaction of the Ru(III)

$$\mathrm{Ru(III)L}_n + \mathbf{7} \rightarrow \underset{\mathbf{8}}{\mathrm{Ru(V)(O)L}_n} + \mathrm{RCO_2H}$$

$$\mathbf{8} + \mathrm{R^1R^2CHOH} \rightarrow \underset{\mathbf{9}}{[\mathrm{R^1R^2{=}OH^+\ Ru(OH)L}_n]}$$

$$\rightarrow \mathrm{Ru(III)L}_n + \mathrm{R^1R^2C{=}O} + \mathrm{H_2O}$$

complex with the peracid **7** would give Ru(III)OOCOR which undergoes cleavage of the O–O bond to give the oxoruthenium(V) intermediate **8**.[15,16] Abstraction of a hydrogen and subsequent electron transfer would give intermediate **9**, which collapses to give Ru(III), carbonyl compounds, and water to complete the catalytic cycle.

Work is in progress to provide definitive mechanistic information and to apply the present method to other systems.

Supplementary Material Available: Experimental procedures and spectral data for product ketones and carboxylic acids (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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