Selective Catalytic Oxidation of Alcohols by a Ruthenium-Copper Bifunctional System Using Molecular Oxygen

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The oxidation of allylic and benzylic alcohols to aldehydes can be carried out at room temperature with molecular oxygen, in the presence of the bifunctional ruthenium-copper system (nPr$_4$N)(RuO$_4$)–CuCl acting as the catalyst.

The oxidation of alcohols to aldehydes and ketones is a fundamental reaction in organic synthesis, and numerous oxidizing reagents are available to effect this key transformation.[1] In most instances, these reagents are used in stoichiometric amounts and are very often toxic such as the chromium oxidants used in vast amounts in both the laboratory and industry.[1] However, with the ever-growing environmental and economic concerns the development of catalytic processes for alcohol oxidation is becoming increasingly important.

A particularly noteworthy process has been described by Griffith et al.[2] who reported the use of the high oxidation state oxoruthenium compound tetra-*n*-propylammonium perruthenate (nPr$_4$N)(RuO$_4$), TPAP, as a mild catalyst for the oxidation of alcohols with *N*-methylmorpholine *N*-oxide, NMO, as the secondary oxidizing source. More recently, we reported the catalytic oxidation of primary alcohols to aldehydes with *cis*-dioxymolybdenum(VI) complexes and sulfoxides as the co-oxidant.[3] Although both of the above function well as catalytic systems, unpleasant and harmful by-products, amine and sulfide respectively, are produced. This limits the use of these catalysts on an industrial scale. The quest for catalytic systems that use inexpensive, nontoxic, molecular oxygen in the air as the secondary oxidant remains a particularly important goal for the development of a "green method" for converting alcohols to carbonyl products on an industrial scale.[4]

Relatively few ruthenium-based catalytic systems using air or molecular oxygen have been reported for the dehydrogenation of alcohols. These include the trinuclear ruthenium carboxylates $[Ru_3O(O_2CR)_6L_3]^n$ ($R = CH_3$ or C_2H_5; $L = H_2O$ or PPh_3; $n = 0, +1$)[5], the ruthenium(II) species $[RuCl_2(PPh_3)_3]$[6], $RuO_2 \cdot xH_2O$[7], the binuclear $[Ru_2O_6(C_5H_5N)_4] \cdot 3.5H_2O$[8], the bimetallic system $RuCl_3-Co(OAc)_2$[9] and the triple catalytic system [RuCl(OAc)(PPh$_3$)$_3$]−hydroquinone−[Co(salophen)(PPh$_3$)][10] where H$_2$salophen = *N,N'*-bis(salicylidene)-*O*-phenylenediamine. However, these catalysts are rarely selective and are often limited as rather high reaction temperatures and high pressures of molecular oxygen are required and low turnover numbers are observed.

Recently, during the preparation of our manuscript Ley[11] and Markó[12] have communicated the use of tetra-*n*-propylammonium perruthenate, (nPr$_4$N)(RuO$_4$), in the presence of molecular oxygen, as a catalytic oxidant of both primary and secondary alcohols. Markó[12] has also observed that the presence of CuCl · phenanthroline (5 mol-%) and K_2CO_3 (200 mol-%) produced a retarding effect in the oxidation of 4-chlorobenzyl alcohol. We wish to communicate some of our recent results on a similar (nPr$_4$N)(RuO$_4$)−CuCl bimetallic system which is a selective and efficient catalytic system for the oxidation of alcohols with molecular oxygen under mild conditions (25°C), producing water as the only stoichiometric by-product, Scheme 1.

The catalytic oxidation of various alcohols takes place smoothly at 25°C with (nPr$_4$N)(RuO$_4$) (1 mol-%), CuCl (1 mol-%), and 2-aminopyridine (5 mol-%) in the presence of 1 atm of molecular oxygen in toluene, dichloromethane, or acetonitrile. The results are presented in Table 1. The addition of powdered 4-Å molecular sieves results in slightly increased rates, as previously observed in oxidations with (nPr$_4$N)(RuO$_4$) and NMO.[2] This may be because the water formed as a by-product in the reaction degrades the catalyst. Allylic and benzylic alcohols are oxidized with nearly

Scheme 1

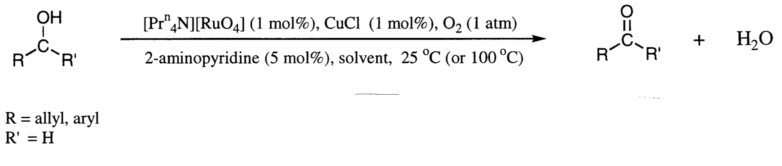

Table 1. Oxidation of alcohols to carbonyl compounds catalysed by a ruthenium−copper bifunctional system[a]

Entry	Substrate	*t* [h]	Product	Yield[b] (%)	Selectivity (%)
1	$4\text{-MeOC}_6\text{H}_4\text{CH}_2\text{OH}$[c][d]	24	$4\text{-MeOC}_6\text{H}_4\text{CHO}$	5[e]	56
2	$4\text{-MeOC}_6\text{H}_4\text{CH}_2\text{OH}$[c]	17	$4\text{-MeOC}_6\text{H}_4\text{CHO}$	100	100
3	$4\text{-MeOC}_6\text{H}_4\text{CH}_2\text{OH}$[c][f]	27	$4\text{-MeOC}_6\text{H}_4\text{CHO}$	50	100
4	$4\text{-MeOC}_6\text{H}_4\text{CH}_2\text{OH}$[g]	25	$4\text{-MeOC}_6\text{H}_4\text{CHO}$	71	100
5	$4\text{-MeOC}_6\text{H}_4\text{CH}_2\text{OH}$[h]	24	$4\text{-MeOC}_6\text{H}_4\text{CHO}$	61	100
6	$4\text{-MeOC}_6\text{H}_4\text{CH}_2\text{OH}$	23	$4\text{-MeOC}_6\text{H}_4\text{CHO}$	52	100
7	$4\text{-ClC}_6\text{H}_4\text{CH}_2\text{OH}$	26	$4\text{-ClC}_6\text{H}_4\text{CHO}$	40	100
8	$4\text{-CF}_3\text{C}_6\text{H}_4\text{CH}_2\text{OH}$	26	$4\text{-CF}_3\text{C}_6\text{H}_4\text{CHO}$	41	100
9	$2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}_2\text{OH}$	25	$2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CHO}$	51	100
10	$2,6\text{-Cl}_2\text{C}_6\text{H}_3\text{CH}_2\text{OH}$	25	$2,6\text{-Cl}_2\text{C}_6\text{H}_3\text{CHO}$	12	100
11	cinnamyl alcohol[c]	26	cinnamaldehyde	94	100
12	cinnamyl alcohol	29	cinnamaldehyde	47	100
13	$\text{C}_6\text{H}_5\text{CH}_2\text{OH}$	21	$\text{C}_6\text{H}_5\text{CHO}$	61	100
14	$\text{C}_6\text{H}_5\text{CH}_2\text{OH}$[i]	2	$\text{C}_6\text{H}_5\text{CHO}$	90	100
15	$\text{C}_6\text{H}_5\text{CD}_2\text{OH}$[i]	2	$\text{C}_6\text{H}_5\text{CDO}$	41	100
16	2-buten-1-ol	17	2-buten-1-al	53	100
17	2-methyl-2-propen-1-ol	24	2-methyl-2-propen-1-al	32	100
18	1-butanol	43	1-butanal	9	100
19	1-hexanol[c]	24	1-hexanal	1	100
20	1-decanol	50	1-decanal	6	100
21	1-decanol[c]	24	1-decanal	1	100
22	2-butanol	72	2-butanone	1	100
23	L-menthol	72	L-menthone	1	100
24	cyclobutanol[i]	43	cyclobutanone[j]	44	100
25	cyclohexanol	39	cyclohexanone	6	100
26	cyclohexanol[c]	27	cyclohexanone	1	100

[a] General reaction conditions: ($n\text{Pr}_4\text{N}$)(RuO_4) (1 mol-%), CuCl (1 mol-%), 2-aminopyridine (5 mol-%), 0.5 g of powdered 4-Å molecular sieves, 6 ml of dichloromethane, 1 atm of molecular oxygen, and temperature 25°C. − [b] GC determination. − [c] Toluene (6 ml), 100°C. − [d] In the absence of ($n\text{Pr}_4\text{N}$)(RuO_4). − [e] 4% conversion to the corresponding acid. − [f] In the absence of a nitrogen donor ligand. − [g] Acetonitrile (6 ml), 50°C. − [h] Acetonitrile (6 ml), 25°C. − [i] 20 equivalents of substrate. − [j] Determined by ^{1}H-NMR spectroscopy.

total selectivity to aldehydes with no further oxidation to the corresponding acids observed. Slightly improved rates can be observed in toluene at 100°C (***WARNING:*** Attempted oxidation of 1-butanol in toluene at 100°C resulted in an explosion) and acetonitrile at 50°C. The bifunctional ($n\text{Pr}_4\text{N}$)(RuO_4)−CuCl catalyst was found to be very selective, with only benzylic and allylic alcohols undergoing any significant oxidation. Aliphatic primary alcohols such as 1-butanol (entry 18) and 1-decanol (entry 20) remain effectively unchanged under the same conditions at 25°C in dichloromethane or acetonitrile, and increasing the temperature to 100°C with toluene as the solvent has little effect (entry 21). Similarly, secondary alcohols were found to undergo very little oxidation (cyclohexanol, entry 25 and 26) or not at all (2-butanol, entry 22 and L-menthol, entry 23), a notable exception being cyclobutanol (entry 24) which was slowly oxidised in dichloromethane. We believe that the dehydrogenation of cyclobutanol results from it being less sterically encumbered than other more common secondary alcohols. The oxidation reactions, therefore, appear to be sensitive to steric factors near the alcohol functional group. This is further supported by the increase in rate of oxidation of 2,4-dichlorobenzyl alcohol (entry 9) compared with 2,6-dichlorobenzyl alcohol (entry 10). This has been observed in the ($n\text{Pr}_4\text{N}$)(RuO_4)/NMO system[2] but it would seem to a lesser degree, as a range of secondary alcohols readily undergo oxidation with this system. This suggests that as with the ($n\text{Pr}_4\text{N}$)(RuO_4)/NMO system, the bifunctional ($n\text{Pr}_4\text{N}$)(RuO_4)−CuCl reagent is sterically demanding, with oxidation presumably occurring through the intermediacy of ruthenate esters. The selectivity of the ruthenium-copper catalyst is significantly different to that of the Griffith ($n\text{Pr}_4\text{N}$)(RuO_4)/NMO system[2] and the ($n\text{Pr}_4\text{N}$)(RuO_4)/O_2 system of Ley[11] and Markó[12], where benzylic, allylic and aliphatic primary alcohols and secondary alcohols are all readily oxidized. As with the Griffith, Ley, and Markó systems, functional groups such as double bonds remain intact during the oxidations.

The role of the copper compound is unclear. Varying the copper complex used in the system from CuCl to $\text{Cu(OCOCH}_3)_2$, CuO, or $[\text{Cu(MeCN)}_4][\text{PF}_6]$ has little effect on the rate of oxidation; CuCl shows marginally improved initial rates. The concentration of the copper complex seems to be significant as the addition of 10 equivalents results only in stoichiometric oxidation. The addition of the nitrogen donor ligand (2-aminopyridine) causes a marked improvement on the rate of oxidation (compare entry 2 and 3). This may be as a result of complexation to the copper complex resulting in a more soluble species which is more efficient in activating or binding the molecular oxygen.[13] UV/Vis spectroscopy and electrospray mass spectrometry preclude any involvement of the nitrogen donor ligand with ($n\text{Pr}_4\text{N}$)(RuO_4). Similar conlusions have been reached for RuO_4 which, unlike OsO_4, is unable to form simple adducts with nitrogen donor ligands.[8][14]Varying the nitrogen donor ligand from 2-aminopyridine to pyridine, 4-dimethylaminopyridine, or 2,6-lutidine has little effect on the rate of oxidation. However, addition of a bidentate nitrogen donor ligand, e.g. 2,2′-bipyridyl results in a decrease in catalytic activity as also noted by Markó.[12]

The observation that cyclobutanol is oxidized to cyclobutanone with total selectivity (entry 24) by this bifunctional catalyst would suggest one-electron processes are not involved in the oxidation process.[15] Similarly, studies on the oxidation of a series of *para*-substituted benzyl alcohols $RC_6H_4CH_2OH$ [R = OMe (entry 6), Cl (entry 7), CF_3 (entry 8), and H (entry 13)] show no correlation with Hammett σ parameters. Hence, benzyl radicals would appear not to be involved in the catalytic process, a conclusion which is further supported by the observation that radical traps, such as 2,4,6-tri-*tert*-butylphenol, have no effect on the rate of oxidation. In kinetic isotope effect experiments, the overall rate of the catalytic oxidation of $C_6H_5CH_2OH$ (entry 14) and $C_6H_5CD_2OH$ (entry 15) in parallel experiments yields the value of $k_H/k_D = 2.2$, indicating that C−H cleavage is involved in the rate-determining step. The nature of the action of the bifunctional ruthenium−copper catalyst is unclear and is currently under further investigation.

Finally, we have found that both the simple $(n\mathrm{Pr}_4\mathrm{N})(\mathrm{RuO}_4)/\mathrm{O}_2$ and $(n\mathrm{Pr}_4\mathrm{N})(\mathrm{RuO}_4)/\mathrm{Cu}/\mathrm{O}_2$ systems give very dark heterogeneous solutions during catalysis. Preliminary experiments seem to indicate the formation of colloidal material in these reactions. We have used different separation methods (e.g. centrifuging and membrane filtration) to remove the major part of the solid material formed. However, the residual solution contains particulate matter (ca. 200 nm, determined by photo correlation spectroscopy) and, interestingly, is still catalytically active. Therefore, whether the catalysis occurs heterogeneously or homogeneously remains unknown. Studies on more stable bifunctional systems are underway to clarify this point.

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Experimental Section

General: Most of the reagents were used without further purification except for the solvents, dichloromethane, acetonitrile, and toluene, which were dried and distilled prior to use. The catalyst $(n\mathrm{Pr}_4\mathrm{N})(\mathrm{RuO}_4)$ and all the substrates described in Table 1 were purchased from Aldrich Chemicals or Lancaster Synthesis. The analyses of the catalytic reactions were carried out with a Hewlett Packard 5890 Series II Gas Chromatograph equipped with a flame ionisation detector (FID) and a methyl silicone gum column of length 10 m, diameter 0.53 mm and 2.65 µm film thickness. ^{1}H-NMR spectra were recorded with a Bruker AC300 spectrometer and referenced internally to TMS.

General Procedure for the Oxidation of Alcohols: In a typical oxidation experiment the alcohol (100 mol-%) and 2-aminopyridine (5 mol-%) were dissolved in dichloromethane (6 ml), and powdered 4-Å molecular sieves added. After stirring the mixture for 10 min at 25°C under an atmosphere of molecular oxygen the copper complex (1 mol-%) was added followed by $(n\mathrm{Pr}_4\mathrm{N})(\mathrm{RuO}_4)$ (1 mol-%). The reaction was monitored by GC, with each sample taken from the reaction first filtered through a small plug of silica gel and washed with diethyl ether to remove any metal compounds.

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[1] B. M. Trost, I. Fleming (Eds.), *Comprehensive Organic Synthesis*, **1991**, vol. 7 ("Oxidation"), Pergamon Press, UK; W. J. Mijs, C. R. H. I. De Jonge (Eds.), *Organic Synthesis by Oxidation with Metal Compounds*, Plenum Press, New York, **1986**.

[2] W. P. Griffith, S. V. Ley, G. P. Whitcombe, A. D. White, *J. Chem. Soc., Chem. Commun.* **1987**, 1625−1627; W. P. Griffith, S. V. Ley, S. P. Marsden, J. Norman, *Synthesis* **1994**, 639−666.

[3] C. Y. Lorber, J. A. Osborn, I. Pauls, *Bull. Soc. Chim. Fr.* **1996**, *133*, 755−758.

[4] S. M. Brown, P. R. Giles, I. E. Markó, M. Tsukazaki, C. J. Urch, *Science* **1996**, *274*, 2044−2046.

[5] C. Bilgrien, S. Davies, R. S. Drago, *J. Am. Chem. Soc.* **1987**, *109*, 3786−3787.

[6] S. Ito, M. Matsumoto, *J. Chem. Soc., Chem. Commun.* **1981**, 907−908.

[7] M. Matsumoto, N. Watanabe, *J. Org. Chem.* **1984**, *49*, 3435−3436.

[8] A. C. Dengel, A. M. El-Hendawy, W. P. Griffith, C. A. O′Mahoney, D. J. Williams, *J. Chem. Soc., Dalton Trans.* **1990**, 737−742.

[9] N. Hirai, S.-I. Murahashi, T. Naota, *J. Org. Chem.* **1993**, *58*, 7318−7319.

[10] J.-E. Backvall, R. L. Chowdhury, U. Karlsson, *J. Chem. Soc., Chem. Commun.* **1991**, 473−475.

[11] R. Lenz, S. V. Ley, *J. Chem. Soc. Perkin Trans 1* **1997**, 3291−3292.

[12] S. M. Brown, I. Chellé-Regnaut, P. R. Giles, I. E. Markó, M. Tsukazaki, C. J. Urch, *J. Am. Chem. Soc.* **1997**, *119*, 12661−12662.

[13] G. Davies, M. A. El Sayed, R. E. Fasano, *Inorg. Chim. Acta* **1983**, *71*, 95−99.

[14] M. El-Hendawy, W. P. Griffith, M. N. Moussa, F. I. Taha, *J. Chem. Soc., Dalton Trans.* **1989**, 901−906.

[15] W. P. Griffith, *Chem. Soc. Rev.* **1992**, *21*, 179−185.

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