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Polymer Incarcerated Ruthenium Catalyst for Oxidation of Alcohols with Molecular Oxygen

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Dedicated to Professor Masakatsu Shibasaki on the occasion of his 60th birthday.

Abstract: A polymer incarcerated ruthenium (PI Ru) catalyst for the oxidation of alcohols with molecular oxygen has been developed. The catalyst was prepared from a polystyrene-based copolymer with ruthenium chloride hydrate as the metal source. The choice of ruthenium species was important to obtain high catalytic activity as well as for the suppression of leaching of ruthenium. In the presence of 5 mol% of PI Ru and 15 mol% of 2,2,6,6-tetramethylpiperidine *N*-oxyl (TEMPO), alcohols were oxidized using molecular oxygen at atmospheric pressure to afford the corresponding aldehydes or ketones in good to excellent yields. The catalyst could be recovered and reused at least ten times without loss of activity.

Keywords: heterogeneous catalysis; immobilization; oxidation; ruthenium

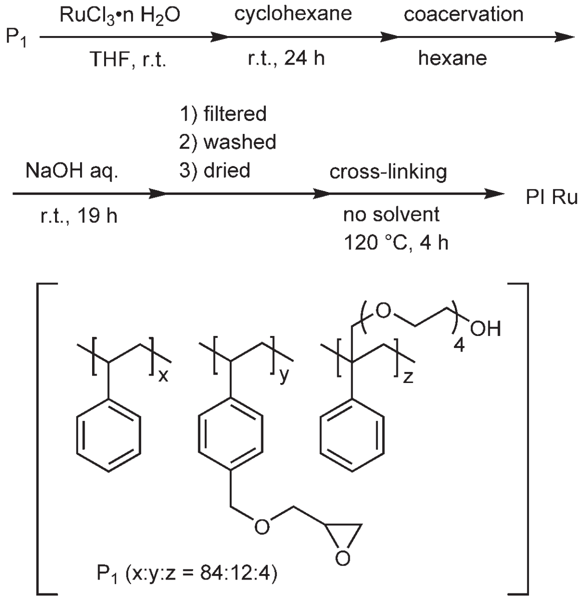
The oxidation of alcohols to carbonyl compounds is one of the most important transformations in organic synthesis.[1] In particular, the selective oxidation of primary alcohols to the corresponding aldehydes plays a central role not only in research laboratories but also in chemical industries. As a result of growing concerns about environmental issues in science, much attention has been paid of late to the development of procedures for this transformation which utilize a metal catalyst and molecular oxygen system in place of the stoichiometric inorganic oxidants associated with traditional oxidation protocols.[2] In this connection, a number of solid supported catalysts, especially ruthenium-based catalysts, have been investigated in recent years.[3]

Recently we developed a novel immobilization technique for metal catalysts, the polymer incarcerated (PI) method,[4] based on microencapsulation and cross-linking, and showed that it could be applied to reactions in efficient catalytic gas-liquid-solid reactions utilizing microchannel reactors.[5] The PI method was also applied to the immobilization of dichlorotris(triphenylphosphine)ruthenium [$RuCl_2(PPh_3)_3$] in both batch and flow systems.[6a] The catalyst was effective for the oxidation of alcohols and sulfides using *N*-methylmorpholine *N*-oxide (NMO) as a co-oxidant. In this context, we decided to investigate the oxidation of alcohols under an atmospheric pressure of molecular oxygen combined with a polymer incarcerated ruthenium (PI Ru) in a batch reactor. Herein we report a practical PI Ru catalyst for the oxidation of alcohols with molecular oxygen to afford the corresponding aldehydes and ketones.

First we prepared the polymer–micelle incarcerated ruthenium catalyst system from copolymer (**P_1**) and $RuCl_2(PPh_3)_3$ in a THF/cyclohexane/hexane system according to the procedure developed by our group.[6b] The catalytic activity of the system was confirmed by examining the oxidation of 4-methoxybenzyl alcohol. Accordingly we conducted the reaction in the presence of 2,2,6,6-tetramethylpiperidine *N*-oxyl (TEMPO) in the manner of the known efficient Ru/TEMPO-catalyzed aerobic oxidation system.[7] Gratifyingly, the reaction proceeded to afford the corresponding aldehyde, with no overoxidation to 4-methoxybenzoic acid. This last observation is assumed to be due to the antioxidant activity of the TEMPO added to the system. However, at this stage the catalytic activity was still not satisfactory and this, coupled with leaching of the Ru (detected by ICP analysis of the reaction filtrate), led as to design a new immobilized catalyst to solve these problems.

Accordingly, we selected ruthenium chloride hydrate ($RuCl_3{\cdot}nH_2O$) as the metal source, and found that it could also be successfully immobilized using the PI method. The preparation of PI Ru from

$RuCl_3 \cdot n\,H_2O$ was conducted based on a modified standard method for the preparation of PI Ru from $RuCl_2(PPh_3)_3$ in which copolymer (**P_1**) was dissolved in tetrahydrofuran (THF) at room temperature, and $RuCl_3 \cdot n\,H_2O$ was added to the solution. Following this, cyclohexane was slowly added to cause coacervation of the metal dispersed in the medium, and the mixture was stirred for 24 h at the same temperature. Hexane was then slowly added and the mixture was left to stand at room temperature for 7 h. The resultant solid was washed with hexane several times and dried at room temperature. Aqueous NaOH (0.5 N) was then added, and the mixture was stirred for a further 19 h at room temperature. Filtration, washing with water and hexane and drying, followed by heating of the catalyst capsules 120 °C for 4 h gave the PI Ru catalyst (Scheme 1). The loading amount of the ruthenium metal was determined by ICP analysis. Treatment with the base before the cross-linking step was effective to suppress the leaching of Ru. Elemental analysis revealed that almost no elimination of chlorine atoms was observed during the preparation of PI Ru.[8]

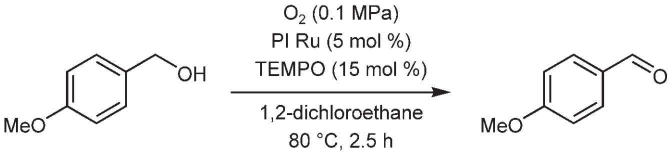


Scheme 1. Preparation of polymer incarcerated ruthenium (PI Ru).

The catalyst obtained using this protocol was used in the oxidation of 4-methoxybenzyl alcohol once again, and the desired aldehyde was obtained in high yield without leaching of Ru (Table 1).

A number of other combinations of monomers in differing ratios to form different copolymers (**P_1**), (for example, more or less hydrophilic copolymers having higher or lower ratios of epoxides and hydroxy groups in the monomers respectively) resulted in decreased catalytic activity.

Table 1. Effect of ruthenium sources.



Entry	Ru source	Conversion [%][a]	Yield [%][a]	Leaching [%][b]
1	$RuCl_3 \cdot n\,H_2O$	>99	96	n.d. (<0.018)
2	$RuCl_2(PPh_3)_3$	57	49	1.19

[a] Determined by GC analysis.

[b] Determined by ICP analysis. Quatitive lower limit is shown in parentheses.

Several examples of oxidation of various kinds of alcohols using the PI Ru prepared from copolymer **P_1** and $RuCl_3 \cdot n\,H_2O$ are summarized in Table 2. Benzyl alcohol derivatives were oxidized to the corresponding aldehydes in high yields (entries 1 to 4). Cinnamyl alcohol and 1-naphthalenemethanol also underwent smooth oxidation in the system (entries 5 and 6). PI Ru was also found to be applicable to the oxidation of heterocyclic alcohols including oxygen and sulfur atoms (entries 7 and 8). The results from entries 4 to 7 demonstrated that leaching of Ru was suppressed in the presence of K_2CO_3. The aliphatic primary alcohol, 1-decanol was converted to the corresponding aldehyde in relatively lower yield (entry 9). The secondary alcohol, (±)-1-phenylethanol was also oxidized, affording the corresponding ketone in 92% yield (entry 10). In the oxidation of an aliphatic secondary alcohol to the corresponding ketone, for example, 2-adamantanone was obtained in 93% yield under the conditions with high catalyst loading (entry 11). ICP was used to detect Ru in the filtrate, and it was found that the leaching level was less than 0.05% when methoxy, methyl and thiophenyl alcohols were used as the substrates (entries 1 to 4 and 8). Slightly higher levels of leaching of Ru were observed in other entries.

Recovery of the catalyst was effected simply and conveniently by filtration of the polymer, followed by washing with dichloromethane and drying. The catalyst so obtained could be reused without any further treatment. In the case of the oxidation of 4-methoxybenzyl alcohol, it was found that no decrease of the yield was observed at all even after we repeated the oxidation reactions ten times, although a slightly longer reaction time was needed to obtain full conversion of the alcohol (Table 3).

In summary, a polymer incarcerated ruthenium catalyst (PI Ru) for the oxidation of alcohols with molec-

Table 2. Oxidation of various alcohols catalyzed by PI Ru.[a]

$$\text{Substrate} \xrightarrow[\substack{\text{1,2-dichloroethane} \\ 80\,^{\circ}\text{C, time}}]{\substack{O_2\ (0.1\ \text{MPa}) \\ \text{PI Ru (5 mol \%)} \\ \text{TEMPO (15 mol \%)}}} \text{Product}$$

Entry	Substrate	Time [h]	Conversion [%][b]	Yield [%][b]	Leaching [%][c]
1	4-Methoxybenzyl alcohol	3	>99	96 [95][f]	<0.017
2	4-Methylbenzyl alcohol	3	>99	99	<0.017
3	2-Methylbenzyl alcohol	3	>99	97	0.048
4	4-Chlorobenzyl alcohol	5 (7)	>99 (>99)	97 (94)	0.68 (<0.027)
5	Cinnamyl alcohol	5 (6)	>99 (>99)	94 (91)	0.72 (0.20)
6	1-Naphthalenemethanol	8 (7)	>99 (>99)	96 (98)	0.22 (<0.046)
7	Furfuryl alcohol	11 (21)	>99 (>99)	91 (90)	0.12 (<0.046)
8	2-Thiophenemethanol	5	>99	94	<0.017
9[d]	1-Decanol	(6)	(92)	(70)	(0.44)
10[e]	(±)-1-Phenylethanol	(21)	(>99)	(92)	(0.16)
11[d,e]	2-Adamantanol	(28)	(>99)	(93)	(0.10)

[a] Unless otherwise stated, the reactions were carried out under atmospheric pressure of O_2 in 0.2 mmol of alcohol. The values shown in parentheses were based on the reactions in the presence of 100 mol% of K_2CO_3.

[b] Determined by GC analysis.

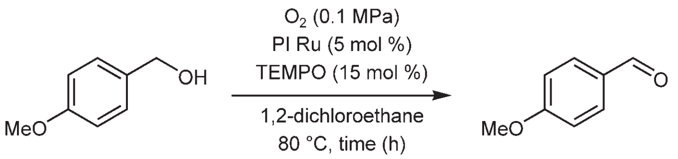
[c] Determined by ICP analysis.

[d] 10 mol% of PI Ru and 30 mol% of TEMPO were used.

[e] The reaction was conducted in chlorobenzene at 100 °C.

[f] Isolated yield is shown in square brackets. The reaction was carried out in a 1.0 mmol scale of the alcohol for 4 h.

Table 3. Recovery and reuse of PI Ru catalyst.[a]



Run	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th
Time [h]	4	6.5	10	10	10	10	10	24	16	12
Conversion [%][a]	>99	>99	>99	>99	>99	>99	>99	>99	>99	>99
Yield [%][b]	98	97	97	97	97	97	98	97	97	97
Leaching [%][c]	0.40	0.33	0.47	0.068	0.049	<0.031	<0.034	0.066	0.038	<0.036

[a] 4-Methoxybenzyl alcohol (0.8 mmol), PI Ru (0.376 mmol g^{-1}, 0.04 mmol), TEMPO (0.12 mmol).

[b] Determined by GC analysis.

[c] Determined by ICP analysis.

ular oxygen has been developed. This catalyst was prepared from $RuCl_3 \cdot nH_2O$ as a metal source and copolymer $\mathbf{P_1}$ for the heterogenization of the catalyst. The oxidation of various alcohols proceeded smoothly to give the corresponding aldehydes and ketones in good to excellent yields. Leaching of Ru was as low as 0.017% and never exceeded 0.72%. The catalyst can be reused at least ten times without loss of activity. Further investigations to apply this system to microchannel reactors are in progress.

Experimental Section

General Remarks

The formation of oxidized compounds (aldehydes and ketones) was confirmed by comparison with commercially available compounds by gas chromatographic (GC) analysis (60 m × 0.25 mm DB-1 column for aldehydes, 60 m × 0.25 mm TC-WAX column for ketones).

Preparation of Copolymer (P_1)

Copolymer (**P$_1$**) was prepared according to the literature procedure.[6b]

Preparation of PI Ru

Copolymer (**P$_1$**) (3.00 g) was dissolved in THF (60 mL) at room temperature, and to this solution was added $RuCl_3 \cdot nH_2O$ (336.0 mg, 40–43 % Ru). Cyclohexane (180 mL) was slowly added to cause coacervation of the metal dispersed in the medium, and the mixture was stirred for 24 h at this temperature. Hexane (420 mL) was then slowly added and the mixture was left to stand at room temperature for 7 h. The resultant solid was washed with hexane several times and dried at room temperature. Aqueous NaOH solution (0.5 N, 300 mL) was then added, and the mixture was stirred for a further 19 h at room temperature. After filtration, washing with water and hexane and drying, the catalyst capsules were heated to 120 °C for 4 h. After filtration, washing with THF, water, acetone and dichloromethane and drying, PI Ru (3.26 g) was obtained. The loading amount of the ruthenium metal was determined by ICP analysis (0.427 mmol g^{-1}).

Oxidation of Alcohols using PI Ru

A typical experimental procedure is described for the oxidation of 4-methoxybenzyl alcohol. 4-Methoxybenzyl alcohol (0.20 mmol), TEMPO (15 mol %), and PI Ru (0.427 mmol g^{-1}, 5 mol %) were combined in 1,2-dichloroethane (0.8 mL) and the mixture was stirred for 3 h under an O_2 atmosphere (0.1 MPa) at 80 °C. At the end of this time, hexane was added to quench the reaction, and the catalyst was collected by filtration and washed with dichloromethane, then dried and reused. The yield of 4-methoxybenzaldehyde was determined by GC analysis with reference to naphthalene as an internal standard.

Metal leaching was determined as follows. After determination of the yield of the reaction, the filtrate was filtered again over celite to remove a portion of fine particles. The solvents were removed under vacuum, and then concentrated sulfuric acid (0.5 mL) was added to this residue. This suspension was heated at 180 °C for 2 h, and then a few drops of nitric acid were added to dissolve insoluble materials, and the mixture was kept at the same temperature for 1 h. The Ru content of solution obtained was used determined by ICP analysis.

Procedure for the Isolatation and Purification of 4-Methoxybenzaldehyde

4-Methoxybenzyl alcohol (137 mg, 1.0 mmol), TEMPO (24 mg, 15 mol %), and PI Ru (0.376 mmol g^{-1}, 133 mg, 5 mol %) were combined in 1,2-dichloroethane, and the mixture was stirred for 4 h under O_2 atmosphere (0.1 MPa) at 80 °C. After hexane was added to quench the reaction, the catalyst was removed by filtration. Solvents were evaporated under reduced pressure, and the crude product was purified by column chromatography (silica gel, hexane/EtOAc) to afford 4-methoxybenzaldehyde; yield: 129 mg (95 %).

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[8] The Ru metal content as determined by ICP analysis was 0.38 mmol g^{-1}. In addition, 1.07 mmol g^{-1}of chlorine atoms were detected by flask combustion-ion chromatograph. This indicates that 2.8 equivs. of chlorine atoms were present in PI Ru.