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# Ruthenium-Catalyzed, One-Pot Alcohol Oxidation–Wittig Reaction Producing α,β-Unsaturated Esters

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**Keywords:** Heterogeneous catalysis / Wittig reactions / Ruthenium / Oxidation

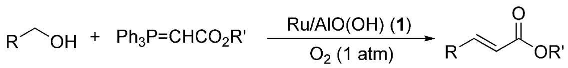
By a one-pot process, α,β-unsaturated esters were synthesized in high yield through the Ru-catalyzed oxidation of primary alcohols and the coupling of the resulting aldehydes and stabilized Wittig reagents. The ruthenium catalyst is composed of ruthenium nanoparticles embedded in aluminum oxyhydroxide and can be recovered simply by filtration or decantation.

## Introduction

The Wittig reaction is an important reaction to provide α,β-unsaturated esters, which are essential intermediates in natural product synthesis.[1] Although the Wittig reaction using aldehydes and phosphorus ylides has a long history,[2] the reaction is limited frequently by the oxidation, decomposition, or polymerization of the aldehydes employed.

Since the discovery of the one-pot Swern oxidation–Wittig reaction reported by Ireland and Norbeck,[3] several methods for the one-pot oxidation–Wittig reaction have been devised.[4–6] However, most of them suffer from the use of hazardous oxidants and/or the requirement of an activation process. For example, Barrett and co-workers used Dess–Martin periodinane, which is not only hazardous but also difficult to handle.[5] Oxidation using manganese dioxide was reported by Taylor and co-workers, which requires preactivation of manganese dioxide.[6] Recently, aerobic oxidation was attempted by Kim and co-workers by using a ruthenium catalyst for the one-pot oxidation–Wittig reaction.[7] However, this system requires stoichiometric $Cs_2CO_3$ and provides alkenyl esters generally in low yields. Meanwhile, Williams and co-workers reported the synthesis of dihydrocinnamate derivatives by a one-pot process, wherein coupling of the resulting aldehydes obtained from dehydrogenation of primary benzylic alcohols with β-carbonyl phosphonates were achieved by using $[IrCl(cod)]_2$ in the presence of base at 150 °C for 72 h.[8] However, the alkenylation products could be isolated and dihydrocinnamate derivatives were obtained as the major products in moderate yields as a result of hydrogenation by iridium hydride intermediates. They have improved the coupling reaction by using a ruthenium N-heterocyclic carbene complex in the presence of vinyltrimethylsilane at 80 °C.[9] However, the major products are still dihydrocinnamate derivatives.

Recently, we developed a method for heterogeneous metal catalysts, which are composed of metal nanoparticles entrapped in highly porous aluminum oxyhydroxide.[10] Among the catalysts, ruthenium catalyst **1** [Ru/AlO(OH)] shows high activity for the dehydrogenation of various alcohols.[10d] Herein, we describe the application of **1** for a one-pot oxidation–Wittig reaction. α,β-Unsaturated esters were obtained in high yield from primary alcohols and stabilized Wittig reagents by using **1** (1 mol-% of Ru) and an oxygen balloon (Scheme 1).



Scheme 1. One-pot oxidation–Wittig reaction.

## Results and Discussion

Catalyst **1** was prepared from ruthenium(III) chloride hydrate, ethanol, and $Al(sec\text{-}OBu)_3$ according to the procedure described previously.[10d] The reaction of benzyl alcohol with methyl (triphenylphosphoranylidene)acetate was carried out under various conditions to find optimum conditions (Table 1). When the reaction was performed by using **1** (1 mol-% of Ru) under an atmosphere of argon, methyl cinnamate and benzyl cinnamate were formed in 59 and 8% yield, respectively, by heating at 110 °C for 30 h (Table 1, Entry 1). However, methyl dihydrocinnamate was

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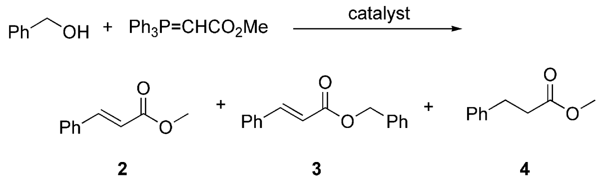
not detected. Notably, changing the reaction atmosphere from argon to oxygen greatly enhanced the reaction efficiency; methyl cinnamate was formed in 91% and the formation of benzyl cinnamate decreased to less than 2% at 80 °C for 20 h (Table 1, Entry 2). The reaction was complete within 12 h at 110 °C with an increased yield of methyl cinnamate (Table 1, Entry 3). The reaction in the air was a little slower than that under an atmosphere of oxygen (Table 1, Entry 4). It is clear that **1** is an excellent catalyst for the one-pot reaction in comparison with commercially available catalysts and those reported for related reactions (Table 1, Entries 5–8); the reaction with the use of **1** is much more selective and faster for the formation of methyl cinnamate than those using other catalysts. In addition, in our reaction system, molecular oxygen was the terminal oxidant and does not require any additives such as base or ligand.

Table 1. Catalytic activity comparison.[a]

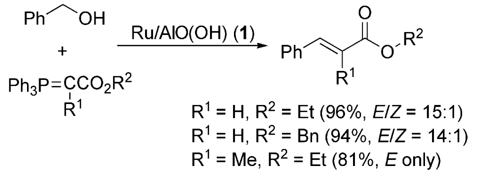


| Entry | Catalyst | $T$ [°C] | $t$ [h] | Yield [%][b] 2 | 3 | 4 |
|---|---|---|---|---|---|---|
| 1[c] | **1** | 110 | 30 | 59 | 8 | 0 |
| 2 | **1** | 80 | 20 | 91 | <2 | 0 |
| 3 | **1** | 110 | 12 | 94 | <2 | 0 |
| 4[d] | **1** | 110 | 12 | 77 | 1 | 0 |
| 5 | 0.5% Ru/$Al_2O_3$[e] | 110 | 12 | 48 | 2 | 0 |
| 6 | 5% Ru/C[e] | 110 | 14 | 77 | 8 | 0.6 |
| 7 | $[IrCl(cod)]_2$[f] | 150 | 72 | 21 | 3 | 68 |
| 8 | $Ru(IMes)(PPh_3)(CO)H_2$[g] | 80 | 24 | | | 78[h] |

[a] A mixture of benzyl alcohol (1.0 mmol), $Ph_3P=CHCO_2Me$ (1.1 mmol), and a catalyst (1 mol-% of Ru) in toluene (2.0 mL) was heated under an oxygen atmosphere (balloon). [b] Determined by $^1H$ NMR spectroscopy. [c] Under an argon atmosphere. [d] In the air. [e] Commercial Ru catalysts. [f] See ref.[8] [g] See ref.[9] [h] Isolation yield.

The recyclability of **1** was tested in the reaction of benzyl alcohol with ethyl (triphenylphosphoranylidene)acetate under the conditions outlined in Entry 3 of Table 1. The catalyst could be recovered simply by decantation, but a decrease in activity was observed with reuse: first use, 93%; second use, 85%; third use, 77%; fourth use, 60%.

We tested three more Wittig reagents for the coupling reaction with benzyl alcohol (Scheme 2). Under the conditions of the Entry 3 of Table 1, ethyl cinnamate and benzyl cinnamate were obtained in 96 (*E*/*Z* = 15:1) and 94% (*E*/*Z* = 14:1) yield, respectively. In the case of the Wittig reagent containing one additional methyl group at the α carbon atom, the reaction was relatively slow and required more catalyst (2.0 mol-% Ru) to give (*E*)-ethyl 2-methyl-3-phenylacrylate in 81% yield. Then, various primary alcohols were employed in the coupling reactions with ethyl (triphenylphosphoranylidene)acetate (Table 2). The expected α,β-unsaturated esters were formed selectively in the reactions of benzylic alcohols as well as aliphatic alcohols, whereas the yields were somewhat low in the reactions of aliphatic alcohols (Table 2, Entries 1 and 2). A substituent effect was not significant in the reactions of benzylic alcohols (Table 2, Entries 3–8). The reaction of 1,4-phenylenedimethanol gave the corresponding diester in 82% yield (Table 2, Entry 7).[11] The vinyl group, which has a capacity to be applied in polymer synthesis, survived during the coupling reaction (Table 2, Entry 8).[12] The carbon–carbon double bond in an allyl alcohol and the triple bond in a propargyl alcohol were also compatible with the reaction conditions (Table 2, Entries 9 and 10). It is notable that the reaction of the propargyl alcohol is much more efficient than that using $[(\eta^6\text{-}p\text{-cymene})RuCl_2]_2$ as a homogeneous catalyst, which gave the corresponding α,β-unsaturated ester only in 28% yield.[7] Our catalyst system was also applicable for the reactions of alcohols containing heteroaromatic rings (Table 2, Entries 11 and 12). The reaction of thiophen-2-ylmethanol was as efficient as those of benzyl alcohols, but that of pyridin-3-ylmethanol was hard to improve.



Scheme 2. Ru-catalyzed, one-pot oxidation–Wittig reaction with benzyl alcohol and stabilized Wittig reagents.

## Conclusions

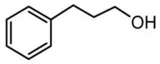
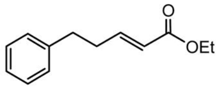
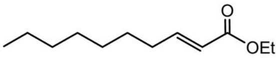
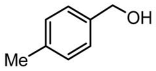
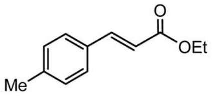
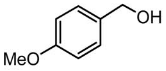
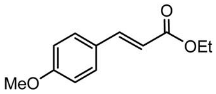
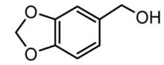
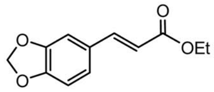
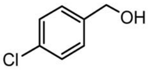
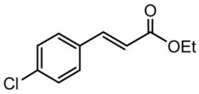
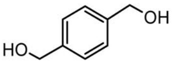
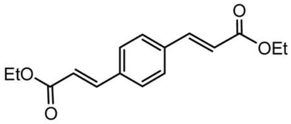
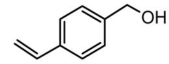
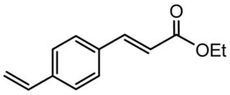
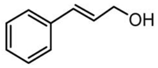
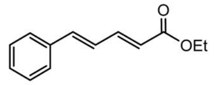
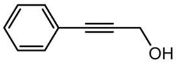
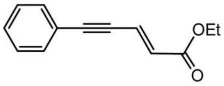
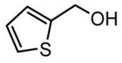
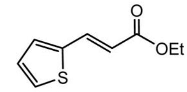
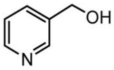
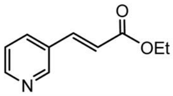
In summary, we have developed a simple and efficient method to prepare α,β-unsaturated esters from primary alcohols and stabilized Wittig reagents through a one-pot process. The method is applicable to aliphatic alcohols as well as benzylic ones and does not require any additives except oxygen, which helps the catalytic dehydrogenation of alcohols.

## Experimental Section

**Synthesis of Ru/AlO(OH) (1):** A mixture of $RuCl_3\cdot 3H_2O$ (Ru content: 41.25%; 130 mg, 0.53 mmol of Ru) and $Al(sec\text{-}OBu)_3$ (9.4 g, 38 mmol) in ethanol (4.6 mL) was heated at 100 °C for 1 h to give a black suspension. Distilled water (9.0 mL) was added into the suspension to give a black gel. The gel was filtered at room temperature, washed with acetone, and dried under an argon atmosphere to give **1** as a gray powder (3.2 g, 1.7 wt.-% of Ru).

**One-Pot Oxidation–Wittig Reaction:** A mixture of benzyl alcohol (100 μL, 1.0 mmol), methyl (triphenylphosphoranylidene)acetate (380 mg, 1.1 mmol), and Ru/AlO(OH) (**1**; 59 mg, 1.0 mol-% of Ru) in toluene (2.0 mL) was stirred for 12 h at 110 °C under an oxygen atmosphere (balloon). The reaction mixture was filtered through a glass filter, and the filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography to give methyl cinnamate (153 mg, 94%).[13]

Table 2. Reactions of ethyl (triphenylphosphoranylidene)acetate and primary alcohols.[a]

| Entry | Alcohol | Product | **1** [mol-% of Ru] | Ylide [mmol] | Time [h] | Yield[b] [%] | *E*/*Z*[c] |
|---|---|---|---|---|---|---|---|
| 1 |  |  | 2 | 1.2 | 25 | 74 | 7:1 |
| 2[d] |  |  | 2 | 1.2 | 24 | 71 | 7:1 |
| 3 |  |  | 1 | 1.1 | 20 | 91 | 29:1 |
| 4 |  |  | 1 | 1.1 | 12 | 97 | 15:1 |
| 5 |  |  | 1.5 | 1.2 | 24 | 95 | 7:1 |
| 6 |  |  | 2 | 1.1 | 12 | 90 | 37:1 |
| 7 |  |  | 2 | 2.2 | 24 | 82[e] | 7:1 |
| 8 |  |  | 2 | 1.2 | 12 | 92 | 15:1 |
| 9 |  |  | 2 | 1.2 | 12 | 85 | 6:1 |
| 10 |  |  | 2.5 | 1.2 | 20 | 73 | 3:1 |
| 11 |  |  | 1 | 1.1 | 12 | 86 | 16:1 |
| 12 |  |  | 2 | 1.2 | 24 | 44 | 7:1 |

[a] A mixture of an alcohol (1.0 mmol), ethyl (triphenylphosphoranylidene)acetate (1.1–2.2 mmol), and **1** in toluene was heated to reflux under an oxygen atmosphere (balloon). [b] The products were isolated by column chromatography. [c] The *E*/*Z* ratio was determined by GC. [d] The reaction mixture was heated at 80 °C. [e] A 87:13 mixture of (*E*,*E*)-diene and (*E*,*Z*)-diene was obtained.

**Supporting Information** (see footnote on the first page of this article): Syntheses of 4-vinylbenzyl alcohol and ethyl 3-(4-vinylphenyl)-acrylate; recycling test for **1**; characterization data for the α,β-unsaturated esters.

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