

Notes

Ruthenium-Catalyzed Oxidation of Secondary Alcohols Assisted by a Simple Alkene

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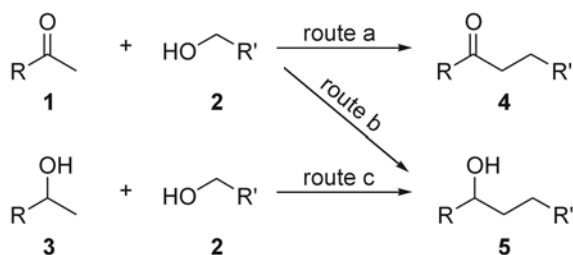
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The oxidation of alcohols to carbonyl compounds has been recognized as a fundamental organic transformation in synthetic organic chemistry. Besides conventional routes, many elegant transition metal-catalyzed methods assisted by co-oxidants are known and used for such transformations.^{1,2} As part of our ongoing studies on ruthenium catalysis, it has recently been found that carbonyl compounds are coupled with alcohols in several routes.³⁻⁵ The coupling of ketones **1** with primary alcohols **2** preferentially afforded coupled ketones **4** (Scheme 1, route a)³ or coupled secondary alcohols **5** (Scheme 1, route b)⁴ according to the molar ratio of **2** to **1**. In addition, secondary alcohols **3** was also found to be coupled with **2** to give **5** (Scheme 1, route c).⁵ Among them, in connection with this report, the addition of sacrificial hydrogen acceptor (1-dodecene) in the case shown in route c of Scheme 1 was essential for the dramatic enhancement of reaction rate.⁵⁻⁷ This could be due to the acceleration of initial oxidations of both starting alcohols by transfer hydrogenation from alcohols to 1-dodecene.⁸ Under these circumstances, this report describes a ruthenium-catalyzed oxidation of secondary alcohols in the presence of 1-dodecene.

The results of several attempted oxidations of 1-(2-naphthyl)ethanol (**3a**) to 2'-acetonaphthone (**4a**) under several conditions are listed in Table 1. Treatment of **3a** in the presence of a catalytic amount of RuCl₂(PPh₃)₃ (2 mol%) along with KOH in dioxane at 100 °C afforded **4a** in 15% isolated yield with 35% conversion of **3a** (run 1). However, when 1-dodecene was further added, the oxidation rate was remarkably enhanced and **4a** was formed in 77% yield with



Scheme 1

Table 1. Oxidation of **3a** into **4a** under several conditions^a

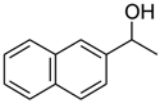
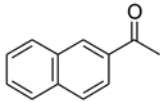
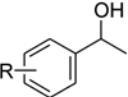
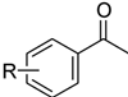




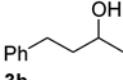
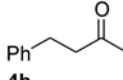
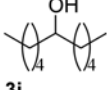
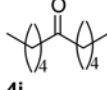
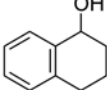
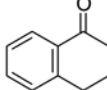
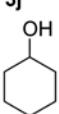
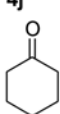
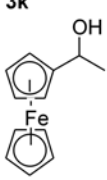
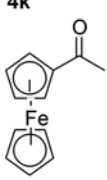
Run	Additive	Base	Solvent	Temp (°C)	Conv. of 3a (%)	Yield (%) ^b
1	—	KOH	dioxane	100	35	15
2	1-dodecene	KOH	dioxane	100	85	77
3	1-dodecene	KOH	dioxane	80	81	71
4	1-dodecene	K ₂ CO ₃	toluene	80	43	41
5 ^c	1-dodecene	KOH	dioxane	80	65	60
6 ^d	benzalacetone	KOH	dioxane	100	89	73

^aReaction conditions: **3a** (1 mmol), RuCl₂(PPh₃)₃ (0.02 mmol), 1-dodecene (5 mmol), base (1 mmol), solvent (2 mL), for 40 h. ^bIsolated yield. ^cRhCl(PPh₃)₃ was used in place of RuCl₂(PPh₃)₃. ^dFor 24 h.

85% conversion of **3a** (run 2). As has been noted in our recent report, the fate of 1-dodecene seems to be partially converted into dodecane by accepting hydrogen.⁵ It is known that the carbon-carbon double bond of α,β -unsaturated carbonyl compound works as a hydrogen acceptor for the ruthenium-catalyzed oxidation of secondary alcohols to ketones.⁹⁻¹¹ Lower reaction temperature (80 °C) resulted in a slightly lower yield of **4a** (run 3). Performing the reaction under K₂CO₃/toluene in place of KOH/dioxane produced **4a** in only 41% yield with incomplete conversion (43%) (run 4). Similar treatment of **3a** in the presence of RhCl(PPh₃)₃ under the employed conditions resulted in lower yield of **4a** (60%) when compared to the use of RuCl₂(PPh₃)₃ catalyst (run 5).

Given the controlled reaction conditions, various secondary alcohols **3** were employed to investigate the reaction scope. The results are summarized in Table 2. Aryl(methyl) carbinols (**3b-3e**) were oxidized into the corresponding ketones (**4b-4e**) in the range of 21-79% yields. The ketone yield was considerably affected by the electronic nature of the substituent on the aromatic ring of aryl(methyl) carbinols. With **3c** and **3d** having electron-donating substituent on the

Table 2. Ruthenium-catalyzed oxidation of secondary alcohols^a

Secondary alcohol 3	Ketone 4	Yield (%) ^b
		77
		41 ^c
3b R = H	4b R = H	79
3c R = 4-Me	4c R = 4-Me	78
3d R = 4-OMe	4d R = 4-OMe	21
3e R = 3-CF ₃	4e R = 3-CF ₃	
		70 ^c
3f	4f	
		34
3g	4g	
		56 ^c
3h	4h	
		36 ^c
3i	4i	
		83
3j	4j	
		31 ^c
3k	4k	
		91
3l	4l	

^aReaction conditions: **3** (1 mmol), RuCl₂(PPh₃)₃ (0.02 mmol), 1-dodecene (5 mmol), KOH (1 mmol), dioxane (2 mL), 100 °C, for 40 h.

^bIsolated yield. ^cGLC yield.

aromatic ring, the ketone yield was generally higher than when **3e** having electron-withdrawing CF₃ substituent on the aromatic ring was used. The oxidation proceeds likewise with alkyl(aryl) carbinol **3f**, but diaryl carbinol **3g** did not oxidize satisfactorily into **4g**. From the oxidations with dialkyl carbinols (**3h** and **3i**), the corresponding ketones (**4h** and **4i**) were also produced in moderate yields. Cyclic carbinols such as 1-tetralol (**3j**) and cyclohexanol (**3k**) were also oxidized into 1-tetralone (**4j**) and cyclohexanone (**4k**), respectively. Here again, as is the case between alkyl(aryl) and dialkyl carbinols, higher reaction rate and yield were observed with benzo-fused cyclic carbinol **3j**. In the case of

1-ferrocenylethanol (**3l**), the oxidation readily occurred under the employed conditions to give acetylferrocene (**4l**).

In summary, a hydrogen transfer oxidation of secondary alcohols has been catalyzed by a ruthenium catalyst in the presence of 1-dodecene as an oxidant (hydrogen acceptor) along with KOH.

Experimental Section

GLC analyses were carried out with a Shimadzu GC-17A instrument equipped with a CBP10-S25-050 column (Shimadzu, fused silica capillary column, 0.33 mm × 25 m, 0.25 μm film thickness) using nitrogen as carrier gas. The isolation of pure products was carried out via thin layer chromatography (silica gel 60 GF₂₅₄, Merck). Commercially available organic and inorganic compounds were used without further purification.

General experimental procedure. A mixture of secondary alcohol (1 mmol), 1-dodecene (0.842 g, 5 mmol), KOH (0.056 g, 1 mmol), and RuCl₂(PPh₃)₃ (0.019 g, 0.02 mmol) in dioxane (2 mL) was placed in a 5 mL screw-capped vial and allowed to react at 100 °C for 40 h. The reaction mixture was filtered through a short silica gel column (ethyl acetate) to eliminate inorganic salts. Removal of the solvent left a crude mixture, which was separated by thin layer chromatography (silica gel, ethyl acetate-hexane mixture) to give ketones. All products prepared by the above procedure were identified by comparison with commercial authentic samples.

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References

- Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, 1981.
- For ruthenium-catalyzed oxidation of alcohols with co-oxidants: (a) Sharpless, K. B.; Akashi, K.; Oshima, K. *Tetrahedron Lett.* **1976**, 2503. (b) Tang, R.; Diamond, S. E.; Meary, N.; Mares, F. *J. Chem. Soc., Chem. Commun.* **1978**, 562. (c) Matsumoto, M.; Ito, S. *J. Chem. Soc., Chem. Commun.* **1981**, 907. (d) Müller, P.; Godoy, J. *Tetrahedron Lett.* **1981**, 22, 2361. (e) Tsuji, Y.; Ohta, T.; Ido, T.; Minbu, H. *J. Organomet. Chem.* **1984**, 270, 333. (f) Yamamoto, Y.; Suzuki, H.; Moro-oka, Y. *Tetrahedron Lett.* **1985**, 26, 2107. (g) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, 46, 3936.
- Cho, C. S.; Kim, B. T.; Kim, T.-J.; Shim, S. C. *Tetrahedron Lett.* **2002**, 43, 7987.
- Cho, C. S.; Kim, B. T.; Kim, T.-J.; Shim, S. C. *J. Org. Chem.* **2001**, 66, 9022.
- Cho, C. S.; Kim, B. T.; Kim, H.-S.; Kim, T.-J.; Shim, S. C. *Organometallics* **2003**, 22, 3608.
- As shown in route a of Scheme 1, the reaction also selectively proceeded toward coupled ketones **4** over coupled secondary alcohols **5** in the presence of 1-dodecene. For instance, treatment of equimolar amounts of acetophenone and benzyl alcohol under RuCl₂(PPh₃)₃ (2 mol%)/KOH (1 equiv.)/1-dodecene (1 equiv.)

- dioxane/80 °C/20 h gave 1,3-diphenylpropan-1-one and 1,3-diphenylpropan-1-ol in 82% and 2% isolated yields, respectively. On the other hand, when the reaction was carried out in the absence of 1-dodecene, 1,3-diphenylpropan-1-one was formed in 70% yield along with considerable amount of 1,3-diphenylpropan-1-ol (14%).
7. For similar enhancement of ruthenium-catalyzed oxidative cyclization between 2-aminobenzyl alcohol and secondary alcohols by the addition of 1-dodecene: Cho, C. S.; Kim, B. T.; Choi, H.-J.; Kim, T.-J.; Shim, S. C. *Tetrahedron* **2003**, *59*, 7997.
 8. For recent reviews on transition metal-catalyzed transfer hydrogenation, see: (a) Zassinovich, G.; Mestroni, G.; Gladiali, S. *Chem. Rev.* **1992**, *92*, 1051. (b) Bäckvall, J.-E.; Chowdhury, R. L.; Karlsson, U.; Wang, G. In *Perspectives in Coordination Chemistry*; Williams, A. F.; Floriani, C.; Merbach, A. E., Eds.; VCH: New York, 1992; pp 463-486. (c) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97. (d) Naota, T.; Takaya, H.; Murahashi, S.-I. *Chem. Rev.* **1998**, *98*, 2599. (e) Palmer, M.; Wills, M. *Tetrahedron: Asymmetry* **1999**, *10*, 2045.
 9. (a) Sasson, Y.; Blum, J. *Tetrahedron Lett.* **1971**, 2167. (b) Regen, S. L.; Whitesides, G. M. *J. Org. Chem.* **1972**, *37*, 1832.
 10. Similar treatment of **3a** in the presence of benzalacetone in place of 1-dodecene afforded **4a** in 73% yield with 89% conversion of **3a** (run 6 of Table 1).
 11. For ruthenium-catalyzed isomerization of allylic alcohols to saturated aldehydes and ketones: Sasson, Y.; Rempel, G. L. *Tetrahedron Lett.* **1974**, 4133.
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