Ruthenium Complex-catalyzed Oxidative Cyclization of 4-Penten-1-ols

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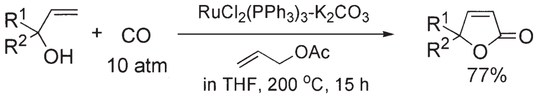
(Received September 25, 2002; CL-020827)

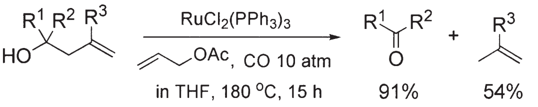
Treatment of 2-phenyl-5-hexen-2-ol (**1a**) with $Ru_3(CO)_{12}$ catalyst and PPh_3 ligand in the presence of allyl acetate and K_2CO_3 in toluene at 160 °C for 20 h under 5 atm of carbon monoxide gave the corresponding oxidative cyclization product, 2,5-dimethyl-2-phenyl-2,3-dihydrofuran (**2a**), in quantitative yield (>99%).

Oxidative addition of protic compounds to low-valent transition-metal complexes is known to give a variety of metal-hydride complexes.[1] The fates of unstable H-[M]-OR species initially formed by an alcohol addition have been studied to discern β-hydrogen elimination,[2] and sometimes a decarbonylation reaction.[3] If the starting alcohols have no β-hydrogens, a stable H-[M]-OR species may be obtained, and it can become a key intermediate in the transition-metal complex-catalyzed transformations of alcohols. For example, we have succeeded in developing novel synthesis of 2(5*H*)-furanons by ruthenium-catalyzed oxidative cyclocarbonylation of 1,1-disubstituted allylic alcohols (Eq 1).[4]



(1)

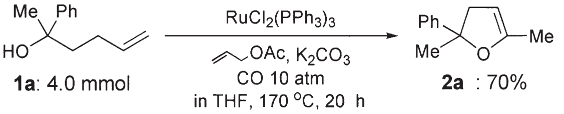
We have also found the ruthenium complex-catalyzed deallylation of 1,1-disubstituted homoallyl alcohols via β-carbon elimination (Eq 2).[5] Thus, the reaction course completely changed, which depends on the length of an alkyl chain in the starting unsaturated alcohols.



(2)

These results have prompted us to examine the reaction of 1,1-disubstituted 4-penten-1-ols (δ,ε-unsaturated alcohols) in the presence of a ruthenium catalyst. Although palladium-catalyzed oxidative cyclizations of 2-allylphenols have been studied in detail,[6,7] only one example of oxidative cyclization of aliphatic δ,ε-unsaturated alcohols has been reported, which gave 2-vinyltetrahydrofurans.[8] Here, we will report novel ruthenium complex-catalyzed oxidative cyclization of 1,1-disubstituted 4-penten-1-ols, which successfully gave 2,3-dihydrofurans in excellent yields.

First, the oxidative cyclization of 2-phenyl-5-hexen-2-ol (**1a**) was attempted by using our previously reported catalyst system of $RuCl_2(PPh_3)_3$ combined with allyl acetate and K_2CO_3[4,9] in THF at 170 °C for 20 h under 10 atm of carbon monoxide to give 2,5-dimethyl-2-phenyl-2,3-dihydrofuran (**2a**) in 70% yield (Eq 3).



(3)

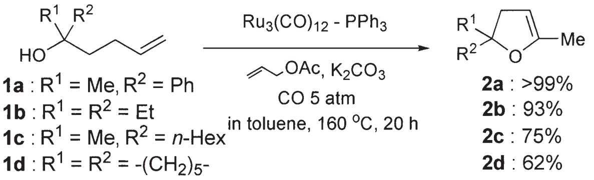
Both allyl acetate and K_2CO_3, as well as carbon monoxide pressure, are essential for the success of the present reaction. Allyl acetate would operate as an effective hydrogen acceptor, but with other hydrogen acceptors, such as styrene, 3,3-dimethyl-1-butene, and vinyl acetate, no reaction occurred at all (vide infra).

Second, we examined the effect of the reaction temperature for the oxidative cyclization of **1a** to **2a**. The present reaction required the temperature over 160 °C. At 180 °C, however, the reaction became sluggish, and no **2a** was obtained, while the conversion of **1a** was almost 100%.

As for the solvent, THF (**2a**, 71%) and hydrocarbon solvents, such as toluene (**2a**, 75%) and mesitylene (**2a**, 74%), gave the good results. However, the solvents of DMF (**2a**, 50%), *N*-methylpiperidine (**2a**, 29%), and acetonitrile (**2a**, 22%), which have high coordination ability, were not suitable for the present reaction. Thus, in toluene at 160 °C for 20 h, the catalytic activity of several ruthenium and other transition-metal complexes was examined (Table 1). The catalytic activity of $RuCl_3 \cdot 3H_2O$ itself (without PPh_3) was quite low (run 3). Addition of 2 equiv. of PPh_3 to ruthenium gave the best result (run 5). Other zero-valent ruthenium complexes combined with PPh_3 generally showed good to high catalytic activity (runs 7–10).[10] Among the other transition-metal complexes, only $RhCl(PPh_3)_3$ showed moderate catalytic activity (run 12).

Since $Ru_3(CO)_{12}$ is commercially available, and has a high catalytic activity when it was used concomitantly with PPh_3 ligand (run 7 in Table 1), $Ru_3(CO)_{12}$ was used as a catalyst in the following experiments. Trialkyl phosphines, such as PCy_3 and PEt_3, and bidentate phosphines, such as dppe, dppp, and dppb, are far less effective than PPh_3. The effect of carbon monoxide pressure was also examined, and ultimately, we found that **2a** was obtained in quantitative yield from **1a** under 5 atm of carbon monoxide.

Under the optimized reaction conditions, several 4-penten-1-ols (**1a**–**c**) were smoothly converted into the corresponding 2,3-dihydrofurans (**2a**–**c**) in high yields. A spiro compound, **2d**, was also prepared by this procedure.[11]



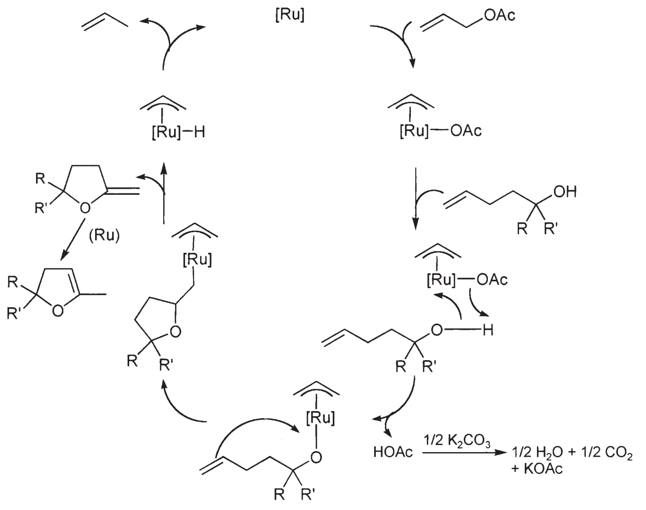
(4)

A most plausible mechanism for the present reaction is illustrated in Scheme 1. Considering of the result that only allyl acetate can operate as an effective hydrogen acceptor for this oxidative transformation (vide supra), initial step of the present reaction might be oxidative addition of allyl acetate to low-valent active ruthenium species.[12] Then, the generated π-allylruthenium intermediate may undergo ligand exchange reaction or σ-bond metathesis between an acetoxyl group with a hydroxyl group to

Table 1. Catalytic Activity of Several Ruthenium and Other Transition-Metal Complexes[a]

Run	Catalyst	Conv. of **1a**/%[b]	Yield of **2a**/%[b]
1	$RuCl_2(PPh_3)_3$	95	75
2	—	7	0
3	$RuCl_3 \cdot nH_2O$	100	38
4	$RuCl_3 \cdot nH_2O + PPh_3$	100	65
5	$RuCl_3 \cdot nH_2O + 2PPh_3$	100	75
6	$RuCl_3 \cdot nH_2O + 3PPh_3$	100	71
7[c]	$Ru_3(CO)_{12}$+$2PPh_3$	95	76
8[d]	$Ru(\eta^4\text{-cod})(\eta^6\text{-cot}) + 2PPh_3$	94	77
9[e]	$Ru(\eta^6\text{-cot})(\eta^2\text{-dmfm})_2 + 2PPh_3$	93	68
10	$Ru(CO)_3(PPh_3)_2$	100	75
11	$Pd(PPh_3)_4$	72	0
12	$RhCl(PPh_3)_3$	100	55

[a] **1a** (4.0 mmol), catalyst (0.20 mmol as a metal atom), allyl acetate (30 mmol), K_2CO_3 (10 mmol), toluene (8.0 mL) under CO (10 atm) at 160 °C for 20 h. [b] Determined by GLC based on the amount of **1a** charged. [c] $Ru_3(CO)_{12}$ (0.067 mmol) and PPh_3 (0.40 mmol). [d] cod = 1,5-cyclooctadiene, cot = 1,3,5-cyclooctatriene. [e] dmfm = dimethyl fumarate.



Scheme 1.

give an (alkoxy)(π-allyl)ruthenium intermediate. Further intramolecular insertion of an alkene moiety into an O-[Ru] bond, followed by β-hydride elimination/isomerization gave 2,3-dihydrofuran, together with the formation of propene.[13] K_2CO_3 acts as a base to neutralize the generated acetic acid.

In conclusion, we have found novel ruthenium-catalyzed oxidative cyclization of 1,1-disubstituted 4-penten-1-ols to 2,3-dihydrofurans. All 2,3-dihydrofurans prepared in this study are new compounds, which are quite attractive as novel functional monomers. Mechanistic study and application of the present reaction to organic synthesis are now under progress.

This work was supported in part by a Grants-in-Aid for Scientific Research (B), and Scientific Research on Priority Areas (A) "Exploitation of Multi-Element Cyclic Molecules" from the Japan Society for the Promotion of Science and the Ministry of Education, Culture, Sports, Science and Technology, Japan. T.K. acknowledges financial support from the UBE Foundation, General Sekiyu Research & Development; Encouragement & Assistance Foundation, and the Yamada Science Foundation.

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10 Under the present reaction conditions, both $RuCl_2(PPh_3)_3$ catalyst and $RuCl_3 \cdot 3H_2O$ catalyst with PPh_3 could be reduced to a common active Ru(0) species, which can explain the effectiveness of these Ru(II) and Ru(III) catalysts as Ru(0) catalysts for the present oxidative cyclization reaction.

11 The reaction using 1,1-disubstituted 4-hexen-1-ols which have methyl substituents on the terminal olefinic carbon, such as 2-phenyl-5-hepten-2-ol, is quite complicated. The yield of normal oxidative cyclization product, 2,5-dimethyl-5-phenyl-4,5-dihydrofuran, was quite low (>5%), while the oxidative cyclocarbonylation on the phenyl substituent occurred to give unexpected 3-methyl-3-(pent-3-enyl)phthalide in 48% yield. Similar oxidative cyclocarbonylation proceeded quantitatively with 1,1-disubstituted 5-hexen-1-ols. Further studies are apparently required for these reactions.

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13 After run 10 in Table 1, a reasonable amount of propene was evolved in the gas phase (4.4 mmol), and we believe that allyl acetate operates as an effective hydrogen acceptor by hydrogenolysis of allyl acetate to propene and acetic acid as in our previous works.[4,9] No propyl acetate, a simple hydrogenated product of allyl acetate, was detected by careful GC analysis.