Transition Metal-Catalyzed Cyclization of 2-Allylphenol to 2,3-Dihydro-2-methylbenzofuran without β-Elimination

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The intramolecular nucleophilic addition of 2-allylphenol was catalyzed by $RuCl_3 \cdot nH_2O/AgOTf–PPh_3–Cu(OTf)_2$ to afford 2,3-dihydro-2-methylbenzofuran in good yield, while 2-(3-butenyl)-phenol was converted to 3,4-dihydro-2(2*H*)-methylbenzopyran.

Nucleophilic addition to olefins by transition-metal catalysts is of great interest, and several processes have already been utilized in industry.[1] Especially, the Wacker process[2] and acetoxylation[3] are important for syntheses of acetaldehyde and vinyl acetate from ethylene, in which nucleophilic attack of hydroxy or acetoxy anions to the ethylene coordinated to Pd is proposed.[4] Interestingly, β-hydride elimination from the intermediate, 2-palladaethanol or its acetate, gave the intended products. On the other hand, if no β-hydride elimination from such an intermediate occur, saturated alcohol derivatives, which are also important industrial compounds, can be obtained directly from olefins under neutral conditions.[5]

Our research interest in the catalytic addition of nucleophiles to olefins without β-hydride elimination induced us to use 2-allylphenol (**1**) as both a nucleophile and an olefin. Generally a strong acid promotes this type of nucleophilic addition to olefins,[6,7] and also photocatalytic reaction of **1** to **2** was reported.[8] On the other hand, intramolecular cyclizations of olefins with hydroxy group such as **1** by palladium catalyst was proceeded via a mechanism including nucleophilic addition and β-hydride elimination proposed in the Wacker reaction.[9–12] Only one report about catalytic cyclization of 5-hexenyl- or 6-heptenyl-ammonium triflate without β-hydride elimination was presented so far,[13] while there were several cyclization reactions with carbonylation instead of β-hydride elimination[14] or using reducing agent for reduction of metal carbon bond.[15] We report here a new catalytic cyclization of 2-allylphenol to 2,3-dihydro-2-methylbenzofuran without β-hydride elimination.

Various catalytic systems and reaction conditions were examined for the cyclization of **1**, and some representative results are listed in Table 1. Ruthenium and iron compounds treated with AgOTf showed some activities for this reaction, while only the ruthenium compound exhibited good catalytic activity with the addition of $Cu(OTf)_2$. Cyclization of **1** was effectively performed in acetonitrile at 80 °C in the presence of a ruthenium-based catalyst prepared by pre-heating a mixture of $RuCl_3 \cdot nH_2O$ and AgOTf (3 eq. to $RuCl_3 \cdot nH_2O$[16]) in CH_3CN to give **2** in moderate yield. Acetonitrile was chosen among the solvents examined. No reaction occurred by use of $AgBF_4$ instead of AgOTf or by addition of $CuCl_2$ instead of $Cu(OTf)_2$.

From the reaction, the desired product **2** was obtained in moderate yield followed by considerable amounts of **3** and olefin-isomerized product **4**. Interestingly, the addition of TfOH or PPh_3 suppressed the formation of **3** and **4**. Since TfOH alone was ineffective as a catalyst for this cyclization, TfOH influenced the catalytic stage mediated by ruthenium.

This catalytic cyclization was not influenced by the substituents on the aromatic ring of the substrate (Table 2), and five-

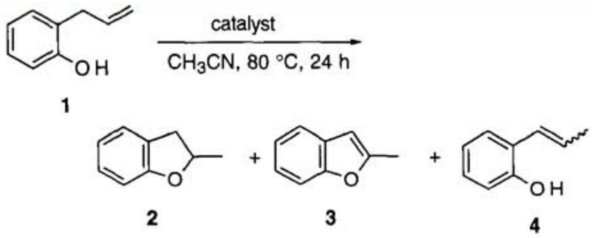
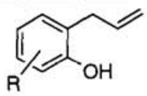
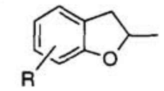
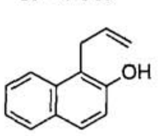
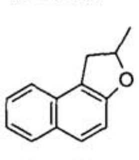
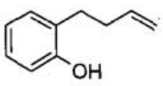
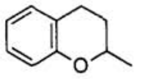


Table 1. Cyclization of **1** by transition-metal catalyst[a]

catalyst	additive	yield (%)[b] 2	3	4
$RuCl_3 \cdot nH_2O$ / 3AgOTf	$Cu(OTf)_2$	51	4	15
$RuCl_3 \cdot nH_2O$ / 3AgOTf	—	4	1	10
$PdCl_2$ / 2AgOTf[c]	$Cu(OTf)_2$	0	4	23
$RhCl_3 \cdot 3H_2O$ / 3AgOTf	$Cu(OTf)_2$	0	trace	5
$FeCl_3 \cdot 6H_2O$ / 3AgOTf	$Cu(OTf)_2$	4	0	10
AgOTf	—	0	0	0
—	$Cu(OTf)_2$[d]	0	0	0
—	TfOH[e]	0	0	0
$RuCl_3 \cdot nH_2O$ / 3AgOTf	$Cu(OTf)_2$ / TfOH[f]	63	0	trace
$RuCl_3 \cdot nH_2O$ / 3AgOTf[g]	$Cu(OTf)_2$ / PPh_3	69	0	2

[a] Reaction conditions: 2-allylphenol (4.0 mmol), $RuCl_3 \cdot nH_2O$ (0.4 mmol), AgOTf (1.2 mmol), $Cu(OTf)_2$ (2.0 mmol), CH_3CN (10 mL), 80 °C, 24 h. [b] Determined by GLC analysis (PEG-20M). [c] CH_3OH (10 mL) as solvent. [d] $Cu(OTf)_2$ (4.0 mmol). [e] TfOH (1.0 mL, 11 mmol). [f] TfOH (0.3 mL, 3.4 mmol). [g] CH_3CN (3 mL), 48 h, PPh_3 (0.8 mmol).

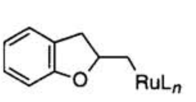
Table 2. Cyclization of 2-alkenylphenol derivatives[a]

substrate	product	yield[b] (%)
		
R = H	R = H	61 (69)[c]
R = 4-MeO	R = 5-MeO	51
R = 6-MeO	R = 7-MeO	53
R = 6-Me	R = 7-Me	65
		58
 **6**		42

[a] Reaction conditions: substrate (4.0 mmol), $RuCl_3 \cdot nH_2O$ (0.4 mmol), AgOTf (1.2 mmol), $Cu(OTf)_2$ (2.0 mmol), PPh_3 (0.8 mmol), CH_3CN (10 mL), 80 °C, 24 h. [b] Isolated yield.[17] [c] Determined by GLC analysis (PEG-20M).

membered ring compounds were always formed from allyl derivatives. 2-Homoallylphenol (**6**) was transformed to a 6-membered cyclic product, 3,4-dihydro-2(2*H*)-methylbenzopyran in moderate yield, while 2-vinylphenol was not converted to the cyclic compound.

Although the mechanism of this reaction is not clear yet, the key intermediate is considered to be **7**. Hosokawa *et al.* also suggested a similar intermediate in the reaction of **1** catalyzed by a Pd compound.[10a] Product **2** could be obtained from **7** by protonolysis, and by-product **3** could be formed from same intermediate **7** by β-hydride elimination. No formation of **3** by addition of TfOH indicates that the protonolysis of **7** proceeds smoothly by adding TfOH. Formation of olefinic by-product **4** was also supressed by adding TfOH or PPh_3, suggesting that **4** was formed from common olefin–ruthenium intermediate via hydrogen migration proposed in the literature.[18]



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Catalytically active species is also not clear. Cationic ruthenium species was considered to be formed from the reaction of $RuCl_3 \cdot nH_2O$ and AgOTf. This cationic Ru(III) species has some TfO^- and acetonitrile molecules. Additional PPh_3 molecules act as a ligand as well. Since addition of 3 eq. of PPh_3 to Ru metal disturbed the reaction, there may be a minimum coordination site on Ru species, when 2 eq. of PPh_3 to Ru atom was added. This could be the reason why the addition of PPh_3 exhibited high selectivity. The role of $Cu(OTf)_2$ was difficult to explain. We think that the catalytically active Ru(III) complexes converted easily to Ru(II) species under the reaction conditions and could be recovered by the reaction of them with $Cu(OTf)_2$. Actually, the amount of $Cu(OTf)_2$ influenced the yields of the products but not the selectivities.

Finally, this new catalyst system, prepared by the heating $RuCl_3 \cdot nH_2O$ and 3 eq. of Ag(OTf) in CH_3CN and then adding $Cu(OTf)_2$, exhibits catalytic activities for intramolecular cyclization of phenol having olefins without β-hydride elimination. This catalysis can open the door for the nucleophilic addition to alkenes without β-hydride elimination under neutral and mild conditions. Further studies of the reaction mechanism, and the scope and application of this reaction are under way.

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