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Ruthenium catalyzed addition reaction of carboxylic acid across olefins without β-hydride elimination

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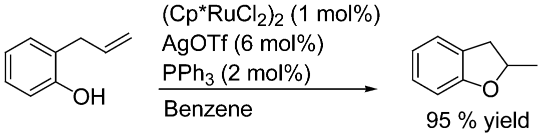
The cationic ruthenium catalyst ($(Cp^*RuCl_2)_2$/AgOTf/Ligand promotes the addition reaction of carboxylic acids across olefins without β-hydride elimination.

Synthetic organic reactions promoted by transition metal complex catalysts have attracted much attention because of their high yields and selectivities. Recently, more efficient organic reactions of the so-called atom economy have been desired from environmental view-point.[1] In general, addition reaction may provide the most "atom-economic" reaction. Moreover, unless the catalytic reactions promoted by transition metal complexes are accompanied by the formation of intractable materials such as inorganic salts, the metal-catalyzed reactions will be useful for synthetic organic transformations, which are suitable for "Green Chemistry".

In the previous paper, we have reported the novel intramolecular cyclization reaction of 2-allylphenol to 2,3-dihydro-2-methylbenzofuran catalyzed by ruthenium complex as below.[2] Of note is that the intramolecular cyclization ends up without involvement of β-hydride elimination. It is contrasted with some transition-metal catalyzed nucleophilic additions to olefins which proceed with β-hydride elimination, as exemplified by the Wacker reaction.[3] Consequently, the transition metal catalysts, which are reduced through the cyclization process, have to be reoxidized to maintain catalytic activity. On the other hand, the present ruthenium-catalyzed cyclization needs no oxidant and gives saturated product in high yield directly with high atom economy.†

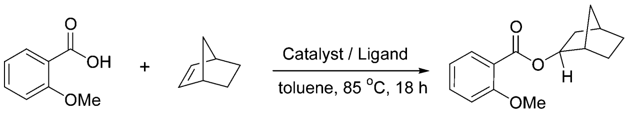


1 **2**

Now our attention has been focused on the intermolecular version of nucleophilic addition of carboxylic acid to olefins, producing carboxylic acid esters. The Ru-catalyzed addition reaction of carboxylic acids to alkynes to give the corresponding vinyl esters were reported by Mitsudo *et al.*,[4] Dixneuf *et al.*[5] and Koley *et al.*[6] Recently, Hartwig and co-workers have reported the hydroamination reaction of styrene derivatives catalyzed by Pd and Ru catalysts.[7] However, the transition-metal-catalyzed addition reaction of the oxygen nucleophiles across olefins, which may involve a common mechanistic feature to the hydroamination reaction, has not been reported. If the title addition reaction proceeds smoothly under mild conditions, it may provide a new entry to regio- and stereo-selective olefin hydration, *i.e.*, the saturated esters produced through the addition reaction undergo selective hydrolysis to give the alcohols together with the corresponding carboxylic acids, which are identical to the starting carboxylic acids, which are reusable as starting materials.

The results of the addition reaction of *o*-anisic acid (**3b**) across 2-norbornene (**4a**) under various conditions are summarized in Table 1. In the absence of ruthenium complex catalyst, no addition reaction took place (entry 1). Treatment of **3b** with **4a** in the presence of 10 mol% of trifluoromethanesulfonic acid (TfOH) under the same conditions gave *exo*- and *endo*-2-norbornyl 2-methoxybenzoates in 29% yield with a ratio of *exo*/*endo* = 75/25 (entry 2). $(Cp^*RuCl_2)_2/2PPh_3$ and $(Cp^*RuCl_2)_2/6AgBF_4/2Ph_3P$ had no catalytic activities (entry 3, 4). However, use of 1.0 mol% of $(Cp^*RuCl_2)_2/6AgOTf/2Ph_3P$ as a catalyst gave *exo*-2-norbornyl(2-methoxy)benzoate (**5b**) in 71% yield (entry 5). Effects of phosphine ligands on the ruthenium complexes are examined, indicating that sterically bulky phosphines increase the product yield. So far,

Table 1 [a]Addition reaction of *o*-anisic acid (**3b**) across 2-norbornene (**4a**)

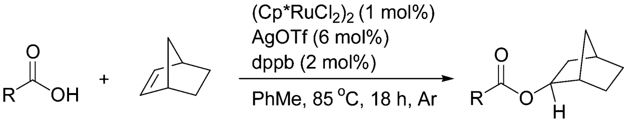


3b **4a** **5b**

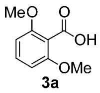
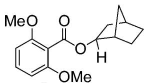
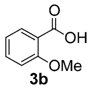
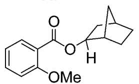
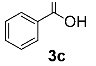
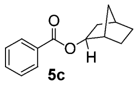
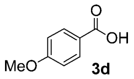
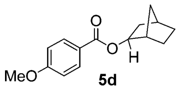
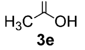
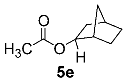
Entry	Catalyst	Ligand	Yield (%)[b]
1	None	None	No reaction
2	TfOH[c]	None	29[d]
3	$(Cp^*RuCl_2)_2$	Ph_3P	0
4	$(Cp^*RuCl_2)_2/6AgBF_4$	Ph_3P	Trace
5	$(Cp^*RuCl_2)_2/6AgOTf$	Ph_3P	71
6	$(Cp^*RuCl_2)_2/6AgOTf$	$(tol)_3$ P	82
7	$(Cp^*RuCl_2)_2/6AgOTf$	dppe	83
8	$(Cp^*RuCl_2)_2/6AgOTf$	dppb	91

[a] Reaction condition; *o*-anisic acid (1.0 mmol), 2-norbornene (1.0 mmol), catalyst (0.01 mmol), ligand (0.02 mmol), PhMe (2.0 mL), at 85 °C, for 18 h, under Ar. [b] Isolated yield based on 2-norbornene. [c] 10 mol% of TfOH was used. [d] *exo/endo* = 75/25.

Table 2 [a]Addition reaction of carboxylic acids across 2-norbornene in the presence of $(Cp^*RuCl_2)_2$/AgOTf/dppb



3a-e **4a** **5a-e**

Carboxylic acid	Product	Yield (%)[b]
 **3a**	 **5a**	63
 **3b**	 **5b**	91
 **3c**	 **5c**	70
 **3d**	 **5d**	90
 **3e**	 **5e**	0

[a] Reaction condition; carboxylic acid (1.0 mmol), 2-norbornene (1.0 mmol), $(Cp^*RuCl_2)_2/4AgOTf/2dppb$ (0.01 mmol), PhMe (2.0 mL), at 85 °C, for 18 h, under Ar. [b] Isolated yield based on 2-norbornene.

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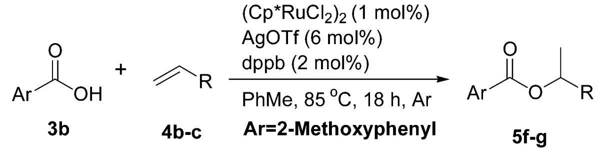
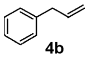
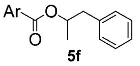
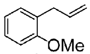
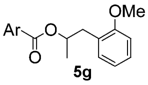
Table 3 [a]Addition reaction of *o*-anisic acids across olefins



Entry	Olefin	Product	Yield (%)[b]
1	 **4b**	 **5f**	0
2			4
3[c]	 **4c**	 **5g**	50

[a] Reaction condition; *o*-anisic acid (1.0 mmol), olefin (1.0 mmol), $(Cp^*RuCl_2)_2$/4AgOTf/2dppb (0.01 mmol), PhMe (2.0 mL), at 85 °C, for 18 h, under Ar. [b] Isolated yield based on olefin. [c] PPh_3 was used instead of dppb.

1,4-diphenylphosphinobutane(dppb) is a ligand of choice in the catalytic reaction (entry 8).

Under the condition described in Table 1 (entry 8), reactions of various carboxylic acids (**3a–3e**) with **4a** were also attempted (Table 2). Benzoic acids with electron-donating group (**3a–b**, **3d**) gave better yields. However, addition reaction of 2,6-dimethoxybenzoic acid (**3a**) with **4a** afforded the corresponding adduct, but in diminished yield (63%), probably due to steric congestion. On the other hand, no reaction took place when acetic acid (**3e**) was used as a starting material, although no reasonable mechanistic explanation was so far given.

However, of note is that only the *exo*-isomer was selectively formed. The stereoselective formation of an *exo*-adduct may suggest that *exo*-ruthenium coordination is crucially important prior to the product formation.

More examples of the addition reaction of carboxylic acids to olefins were shown (Table 3). When allylbenzene (**4b**) was used, no reaction was observed (entries 1). This failure may suggest that stronger π-coordination of 2-norbornene onto ruthenium metal center than the simple terminal olefins might favorably induce the addition reaction. Successful addition of 2-allyl anisole (**4c**) may be due to a possible chelating coordination of the olefin substrate (entry 2). Triphenylphosphine ligand can enhance this chelating effect, increasing the yield of **5g** (entry 3).

In conclusion, novel catalytic addition of benzoic acids with 2-norbornene without accompanying β-hydride elimination was developed. This reaction gave the corresponding esters in good to excellent yields. Moreover, 2-allylanisole gave the corresponding ester in 50% yield. This finding presents a first example of intermolecular addition reaction of carboxylic acid across olefins without β-hydride elimination. The addition reaction coupled with hydrolysis under mild conditions may be useful as an olefin hydration procedure.[8] Further studies on the scope and limitations of the addition reaction as well as the reaction mechanism are now in progress.

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Notes and references

† Typical procedure of addition reaction of carboxylic acids across olefins: $(Cp^*RuCl_2)_2$ (6.2 mg, 0.01 mmol) was dissolved in toluene (2 mL) and the solution was heated to 85 °C. After 15 min, AgOTf (15.5 mg, 0.06 mmol) was added and stirred at 85 °C for 3 h. Dppb (8.6 mg, 0.02 mmol) was added and stirred for 1 h. The reaction mixture was cooled to room temperature. *o*-Anisic acid **3b** (152 mg, 1.0 mmol) and 2-norbornene **4a** (94 mg, 1.0 mmol) were added. The reaction mixture was heated to 85 °C and stirred for 18 h. The crude product was dissolved in diethyl ether (50 mL) and organic layer was washed with water (30 mL, twice), brine (20 mL) and dried over sodium sulfate. The product was purified by silica gel chromatography (hexane/ethyl acetate = 4/1), yielding product **5b** (224 mg, 91%).

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8 Hydrolysis reaction toward the recyclable olefin hydration is in development.