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Addition reaction of 2-phenylbenzoic acid onto unactivated olefins catalyzed by Ru(II)–xantphos catalysis

Yohei Oe [b], Tetsuo Ohta [b,*], Yoshihiko Ito [a]

[a] Department of the Molecular Science and Technology, Faculty of Engineering, Doshisha University, Kyotanabe, Kyoto 610-0394, Japan
[b] Department of Biomedical Information, Faculty of Life and Medical Sciences, Doshisha University Kyotanabe, Kyoto 610-0394, Japan

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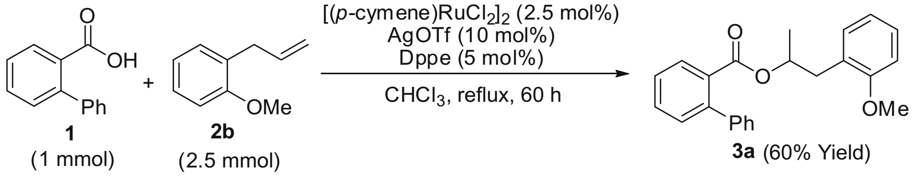
ABSTRACT

Ru(II)–xantphos catalysis is found to be effective for the addition reaction of 2-phenylbenzoic acid onto unactivated olefins. Thus, the reactions of 2-phenylbenzoic acid and unactivated olefins are carried out in the presence of 5 mol % of Ru(II)–xantphos catalysis in refluxing $CHCl_3$ for 48 h to afford the corresponding esters in 40–95% yield. The control experiments indicate that the influence of TfOH for Brønsted acid catalyst was vanishingly small in our new catalytic system.

Esters are one of the most important compounds for pharmaceutics, perfume chemistry and fine chemicals. Esters are also well-known for being converted into the corresponding alcohols and carboxylic acids by saponification and then acidification. The transition metal-catalyzed addition of carboxylic acids onto olefins is one of the most attractive methodologies for ester formations because of its almost perfect atom economy, and therefore, several metal complexes[1–6] were recently reported as efficient catalysts, including our Ru(III) and Ru(II) catalyses.[7] Combining the nature of esters with these catalytic addition reactions of carboxylic acids onto olefin might be considered to be an efficient methodology for the preparation of alcohols from olefins in two steps with recovery of the starting carboxylic acids. Brown's hydroboration–oxidation method[8] is well-known as the most common method for the preparation of alcohols from olefins in two steps, and its asymmetric version[9] has been developed by Knochel and co-workers. However, obtained boron-derived wastes are hardly reusable and not applicable from the view-point of atom efficiency. Thus, if the catalytic addition of carboxylic acids onto olefins becomes more versatile, a new environmentally benign synthetic pathway of alcohols from olefins could be proposed. We have already reported that the ester formations using carboxylic acids and olefins proceeded in the presence of Ru(III) catalyses, though the narrow scope of olefin substrates was problematic.[7a] More recently, we found that the Ru(II) catalyses generated in situ by mixing [(*p*-cymene)$RuCl_2$]$_2$, AgOTf, and DppX showed good catalytic activity for the addition of carboxylic acids, alcohols, and sulfonamides onto styrene in $CHCl_3$, and that [(*p*-cymene)Ru(OTf)(DppX)]OTf were formed as catalytically active complexes for the reaction by NMR experiments, FAB MS spectra, and X-ray analysis.[7c] Furthermore, under these catalytic conditions (DppX = Dppe), the reaction of 2-phenylbenzoic acid (**1**) with 2-allylanisole (**2a**) in the presence of 5 mol % Ru of the catalyst gave 2-{1-(2′-methoxyphenyl)}propyl 2-phenylbenzoate (**3a**) in 60% yield (Eq. 1), though the yield was not satisfied and long reaction time was required. To the best of our knowledge, the reaction temperature (at 61 °C) is the lowest one of the preliminary reported transition metal-catalyzed addition reactions of carboxylic acids onto unactivated olefin described above. The result encouraged us to optimize the reaction conditions to expand the scope of olefin substrates. Herein, we report the recent modification of our Ru-catalyzed addition of carboxylic acid onto various unactivated olefins using xantphos as a ligand, which dramatically increased the catalytic activity.

The bite angle of the bisphosphine ligands is known to be a critical trigger for laying down catalytic activity and reactivity in var-



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[*] Corresponding author. Fax: +81 774 65 6789.
E-mail address: tota@mail.doshisha.ac.jp (T. Ohta).

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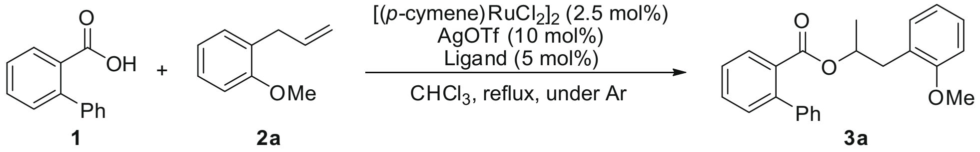
Table 1
Effects of bisphosphine ligands[a]



Entry	Ligand	Bite angle[e] (°)	Time (h)	Yield[b] (%)
1	Dppe	85	60	60
2	Dppp	95	60	80
3	Dpppent	—	60	85
4	Dpph	—	60	82
5	Xantphos	111	24	95
6[c]	Xantphos	111	42	32
7[d]	Xantphos	111	42	64

[a] Reaction conditions: mixture of 2-phenylbenzoic acid (**1**) (1 mmol) and 2-allylanisole (**2a**) (2.5 mmol) was stirred in refluxing $CHCl_3$ (3 mL) for given reaction time in the presence of 5 mol % Ru Catalysis.

[b] Isolated yield after purification by silica gel column chromatography.

[c] Benzoic acid was used instead of **1**.

[d] 2-Phenylpropionic acid was used instead of **1**.

[e] Ref. 13.

ious transition metal-catalyzed reactions.[10] Therefore, the effects of several bisphosphine ligands with different bite angles on the reaction between **1** and **2a** were investigated, and the selected results are summarized in Table 1. When the reaction of **1** with **2a** was performed with Dppe as a ligand at reflux for 60 h, ester **3a** was obtained in 60% yield (entry 1). Changing the ligand to Dppp, which has larger bite angle than Dppe, increases the yield of **3a** to 80% (entry 2), although the reaction time could not be shortened while maintaining good yields. Using Dpppent showed a similar tendency (85% yield, entry 3); however, little decrease in the product yield was observed by using Dpph (82% yield, entry 4). It was expected that the hexane linker was too flexible to maintain a large bite angle on the ruthenium center. On the basis of this hypothesis, xantphos, which has rigid heterocyclic xanthenes promising a large bite angle, was chosen as a ligand.[11] As expected, we were pleased to find that using xantphos increases the product yield up to 95% and that the reaction time could be shortened to 24 h (entry 5). Hartwig and co-workers reported the exchange of the hydroamination product, which was coordinated as an η^6-arene ligand, with the next vinylarene substrate in their *anti*-Markovnikov hydroamination of vinylarenes.[12] They used Dpppent as a ligand for highly efficient reaction, where Dpppent behaves as a P–C–P tridentate ligand to accelerate the exchange reaction. We speculated that similar dissociation or slippage of η^6-*p*-cymene ligand occurred by chelate coordination of xantphos to Ru center to increase the catalytic activity. Benzoic acid and 2-phenylpropionic acid were also reacted with **2a** to afford the corresponding adducts in 32% yield and 64% yield, respectively (entries 6 and 7).

With the effective Ru–xantphos catalytic system in hand, we investigated the scope of olefins by using **1** as a nucleophile, and the selected results are summarized in Table 2. 4-Allylanisole (**2b**) was a good substrate for the present reaction to give 2-{1-(4′-methoxyphenyl)}propyl 2-phenylbenzoate (**3b**) in 95% yield after 48 h (entry 2). When allylbenzene (**2c**) was used as an olefin substrate, the product yield was slightly decreased to afford 2-(1-phenyl)propyl 2-phenylbenzoate (**3c**) in 40% yield (entry 3). Allylbenzene bearing acid-labile acetal substituent (**2d**) can be subjected to the present catalytic system to give a 67% yield of the corresponding ester (**3d**) (entry 4). 4-Phenyl-1-butene (**2e**) was also reacted with **1** to give 2-(4-phenyl)butyl 2-phenylbenzoate (**3e**) in 56% yield (entry 5). Aliphatic olefin, 1-octene (**2f**), gave the desired ester (**3f**) in 89% yield without concomitant of its regio isomers (entry 6). Cyclic olefin, cyclohexene (**2g**) was also applied to the present catalytic reaction with **1** to obtain cyclohexyl 2-phenylbenzoate (**3g**) in excellent yield (89%, entry 7). (*S*)-(−)-Limonene (**2h**) bearing one *gem*-substituted olefin site and one three-substituted cyclic olefin site was not reacted with **1** at the both positions under the present catalytic conditions (entry 8). Methyl *cis*-jasmonate (**2i**), which has an internal (*Z*)-alkene group, also did not afford the corresponding adduct (entry 9). As described above, the present Ru–xantphos catalytic system showed a broad scope of unactivated terminal olefin substrates in the esterification with 2-phenylbenzoic acid.

With the efficient Ru–xantphos catalytic system, we investigated some mechanistic studies. Hartwig and co-workers reported that the reaction of 4-methoxybenzoic acid with 2-norbornene was carried out in the presence of 1 mol % of TfOH in 1,4-dioxane at 80 °C for 22 h to give 2-norbornyl 4-methoxybenzoate in 83% yield.[14] Independently, He and co-workers reported that phenylacetic acid was reacted with 4-allylanisole (**2b**) in the presence of 2 mol % of TfOH in toluene at 50 °C to give the corresponding ester in 60% conversion.[15] Hii and co-workers proposed that their copper-catalyzed hydroamination proceeded by TfOH generated through the ligand exchange reaction of tosylamide with $Cu(OTf)_2$.[16] To confirm the difference between our Ru catalysis and TfOH catalyst, we examined control experiments using TfOH (Eq. 2). Thus, the reaction of **1** with **2b** was conducted in the presence of 1 mol % of TfOH in $CHCl_3$ at reflux or room temperature for 48 h to give the trace amount of

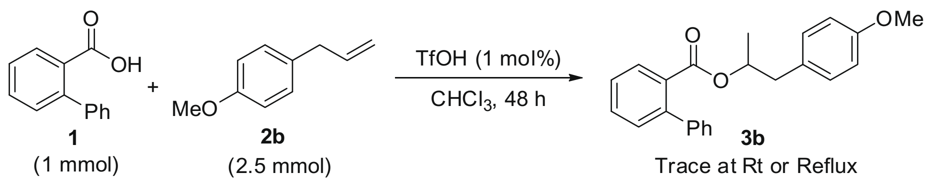


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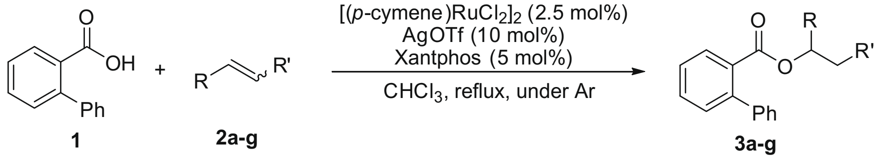
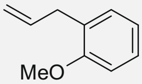
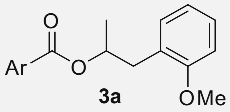
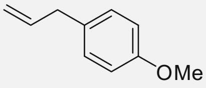
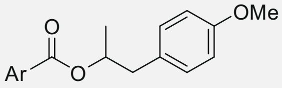
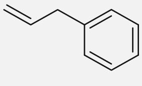
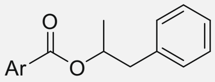
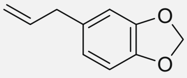
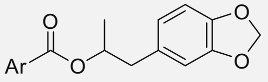
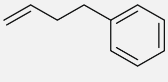
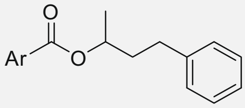
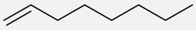
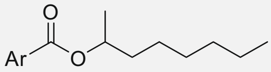
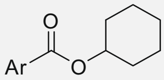
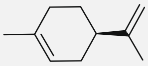
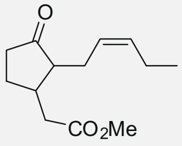
Table 2
Scope of olefin substrates[a]



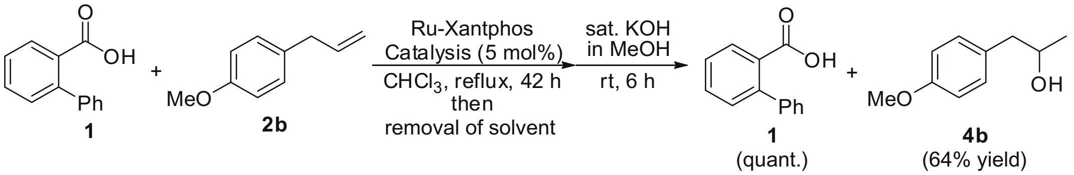
Entry	Olefin	Product[b]	Yield[c] (%)
1	 **2a**	 **3a**	95
2	 **2b**	 **3b**	94
3	 **2c**	 **3c**	40
4	 **2d**	 **3d**	56
5	 **2e**	 **3e**	67
6	 **2f**	 **3f**	89
7	 **2g**	 **3g**	89
8	 **2h**	–	0
9	 **2h**	–	0

[a] Reaction conditions: mixture of 2-phenylbenzoic acid (**1**) (1 mmol) and given olefin (**2**) (2.5 mmol) was stirred in refluxing $CHCl_3$ (3 mL) for 48 h in the presence of 5 mol % of Ru catalysis.
[b] Ar = 2-biphenyl.
[c] Isolated yield after purification by silica gel column chromatography.

esterification product **3b** in both cases. We cannot fully rule out the in situ generated acid-catalyzed reaction pathway from these data; however, this apparent difference of reactivity between TfOH and our Ru–xantphos catalysis indicated that Ru presumably works as a Lewis acid that activates the olefin substrate by forming π–olefin complex like Wacker-type reactions.[17]

Finally, we demonstrated the alcohol preparation process from carboxylic acids and olefins in one-pot using our Ru-catalyzed addition reaction and hydrolysis of the obtained ester (Eq. 3). Thus, the reaction of **1** with **2b** was performed under the present catalytic conditions. After the removal of solvent, treatment of the crude product with saturated KOH methanol solution at room temperature for 6 h afforded the desired alcohol **4b** in 64% yield.[18] As expected, starting acid **1** can be recovered in quantitative yield by acidification followed by simple extraction with ethyl acetate.

In summary, Ru(II)–xantphos catalysis-catalyzed esterification of unactivated olefins using 2-phenylbenzoic acid as a coupling partner was achieved. We also demonstrated an example of one-pot alcohol preparations from olefins by means of the present ruthenium catalytic reaction and followed by hydrolysis, where



(3)

the starting carboxylic acid was quantitatively recovered. The investigations of the addition of optically active carboxylic acids and asymmetric addition using optically active catalysts are under way in our laboratory.

Acknowledgments

We would like to dedicate this Letter to the memory of our mentor, late Professor Yoshihiko Ito. This work was partially supported by Doshisha University's Research Promotion Fund, and a Grant to RCAST at Doshisha University from the Ministry of Education, Culture, Sports, Science and Technology, Japan. This work was supported by a Grant-in-Aid for Young Scientists (Start-up: No. 20850034) from JSPS.

Supplementary data

Supplementary data (typical experimental procedures and copies of ^{1}H and ^{13}C NMR spectra and HRMS of all the products) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.03.052.

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