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Iridium-catalyzed oxidative esterification reaction of aliphatic aldehydes and olefinic alcohols with precoordination of the double bond of alcohols to iridium

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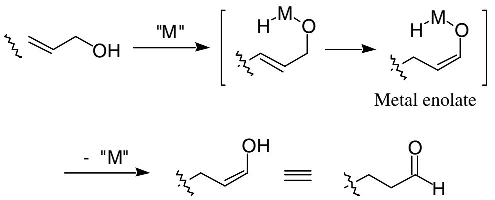
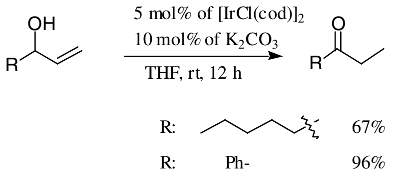
Abstract—A novel iridium-catalyzed oxidative esterification reaction of aliphatic aldehydes and olefinic alcohols in toluene was found under mild conditions of $[IrCl(cod)]_2$ (5 mol %) in combination with K_2CO_3 (10 mol %) at rt.

Iridium complexes are known to be effective for isomerization of allylic alcohols to aldehydes and ketones.[1,2] The transition metal-catalyzed isomerization of allylic alcohols is considered to proceed via the process involving a metal enolate, as depicted in Scheme 1, from the standpoint of the observation of tandem allylic alcohol isomerization aldol reaction.[3,4] On the basis of the mechanism, the possibility and the utilization of atom-economical generation of transition metal enolates can be strongly expected during the isomerization. We started the study of iridium-catalyzed isomerization reaction of allylic alcohols for the purpose of trapping such enolates. At the preliminary stage, we incidentally found the formation of esters in the iridium-catalyzed isomerization reaction of cinnamyl alcohol. We disclose herein a novel iridium-catalyzed oxidative esterification of aliphatic aldehydes with olefinic alcohols.



Scheme 1.

A dramatic rate enhancement by the presence of a catalytic amount of base (K_2CO_3) was observed in ruthenium-catalyzed isomerization of allylic alcohols to saturated ketones.[5] A similar effect of K_2CO_3 was also observed in iridium-catalyzed Oppenauer-type oxidations.[6] While nucleophilic transition metal complexes, like $IrCl(trialkylphosphine)_3$, are known to undergo oxidative addition of alcohols as to give hydrido-alkoxo complexes,[7] the addition was difficult without bases in the case of $[IrCl(cod)]_2$. Thus, we chose mild conditions ($[IrCl(cod)]_2$ (5 mol %), rt, 12 h, THF) in combination with K_2CO_3 (10 mol %) for our iridium-catalyzed allylic isomerization. As expected, secondary allylic alcohols smoothly underwent the isomerization reaction to give the corresponding ketones in good yields (Scheme 2). Primary allylic alcohols, however, exhibited different behaviors. Reaction of cinnamyl alcohol under the same conditions surprisingly gave two types of esters along with a small amount of hydrocinnamaldehyde (Scheme 3). Formation of the esters is formally corresponding to esterification of hydrocinnamic acid with hydrocinnamyl and cinnamyl alcohols. Consequently, the whole process of ester formation must be accounted for by



Scheme 2.

Keywords: $[IrCl(cod)]_2$; Oxidative esterification; Precoordination to olefin.

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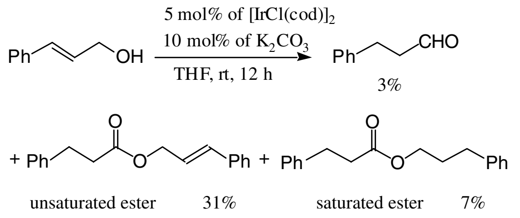
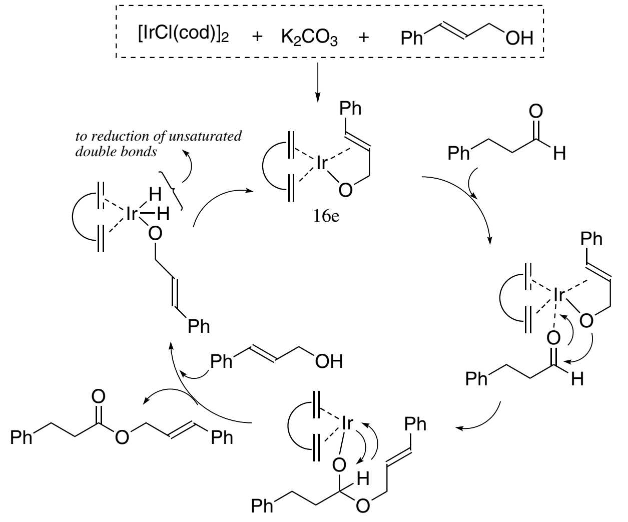


Scheme 3.

C–O bond formation and subsequent oxidation, accompanied by isomerization. Ruthenium-catalyzed oxidative transformation of aldehydes with alcohols to esters was observed at a severely elevated temperature (180 °C).[8] Recently, esters could be formed by insertion of aldehyde into a rhodium alkoxo complex and subsequent β-hydrogen elimination from the resulting alkoxo complex.[9] But, to our knowledge, direct observations of such a condensation between an aldehyde and an alcohol have not been reported yet. A plausible mechanism is shown in Scheme 4. The reaction might initiate with the iridium alkoxo complex formed from $[IrCl(cod)]_2$ and cinnamyl alcohol with assistance of K_2CO_3. The subsequent insertion of the aldehyde, which was in advance produced via isomerization, took place to afford an iridium acetal intermediate, followed by oxidative hydrogen transfer (β-hydrogen elimination)[6,10] to the unsaturated aldehyde in delivering a hydride iridium complex. At the final step the alkoxo complex is recycled to form dihydride species, which can serve some reduction of unsaturated bonds of the product ester and/or the starting alcohol. It is still uncertain whether the cod ligand remains unchanged as it is.[11]

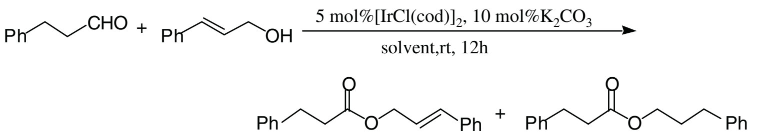


(It is uncertain whether the cod ligand remains unchanged over the whole process)

Scheme 4. A plausible mechanism via insertion of an aldehyde into an alkoxo complex.

The condensation was continuously investigated to realize the general iridium-catalyzed oxidative esterification starting from a primary allylic alcohol and an aldehyde. Reaction of hydrocinnamaldehyde with cinnamyl alcohol resulted in a more good yield, compared with the case of only cinnamyl alcohol (Scheme 3), to give the same ester pair with hydrocinnamyl alcohol (Table 1). The best result in toluene was obtained with a 1:2 molar ratio of the starting aldehyde to alcohol (entry 3). Acetonitrile was inadequate for the reaction, probably owing to its high coordination ability (entry 4). An important limitation was simultaneously found that the reaction with alcohols, not having an olefinic moiety, did not work at all. The precoordination of the olefinic moiety might be essential for this condensation. Iridium-catalyzed allylic isomerization is dispensable for this oxidative esterification. Cross condensation, starting with an allylic alcohol and an aldehyde of different structure, can be considered. In practice, the cross condensation occurred very smoothly (Table 2):[12] Hydrocinnamaldehyde and 2-methylbutyraldehyde were used as typical primary and secondary aliphatic aldehydes. Despite the structural difference of the aldehydes, primary and secondary allylic alcohols underwent the iridium-catalyzed oxidative esterification reaction to afford the corresponding esters (entries 1–5 and 9–11). When secondary alcohols were used, the obtained products were only unsaturated esters (entries 4, 5, and 11). Control experiments clarified an interesting feature of this reaction (entries 6–8) in which olefinic alcohols, having a double bond far from the hydroxy function, exactly worked. Even 5-hexen-1-ol could give the corresponding esters in a satisfactory yield (entry 8). Presumably, the remote double bond also works for the precoordination of

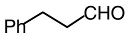
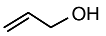
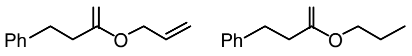
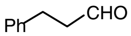
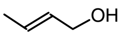
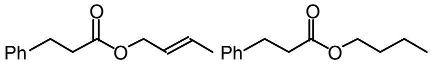
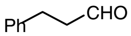
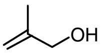
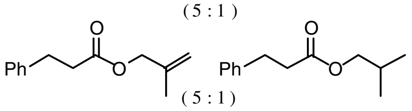
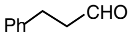
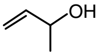
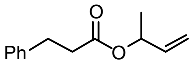
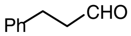
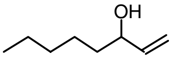
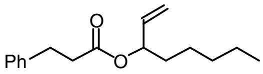
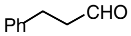
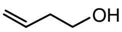
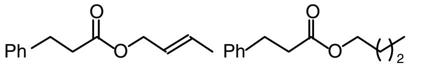
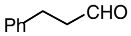
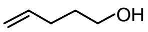
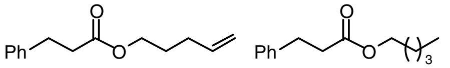
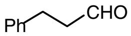
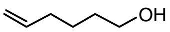
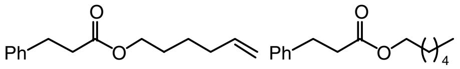
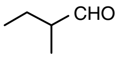
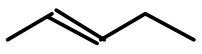
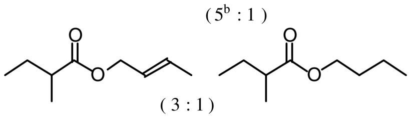
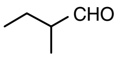
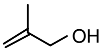
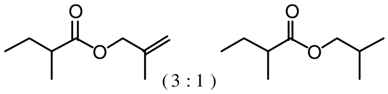
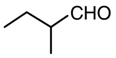
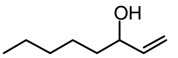
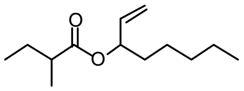
Table 1. Iridium-catalyzed oxidative esterification of hydrocinnamaldehyde with cinnamyl alcohol



Entry	Aldehyde/alcohol	Solvent	% Yield of esters (unsaturated/saturated)
1	1:1	THF	46 (3:1)
2	1:2	THF	60 (2:1)[a]
3	*1:2*	*Toluene*	*97 (3:2)*[a]
4	1:2	CH_3CN	No reaction

[a] The isolated yields were determined, based on the starting aldehyde, although the amount of the aldehyde might be partially increased by isomerization of cinnamyl alcohol during the reaction.

Table 2. Iridium-catalyzed oxidative esterification reaction with a variety of olefinic alcohols[a]

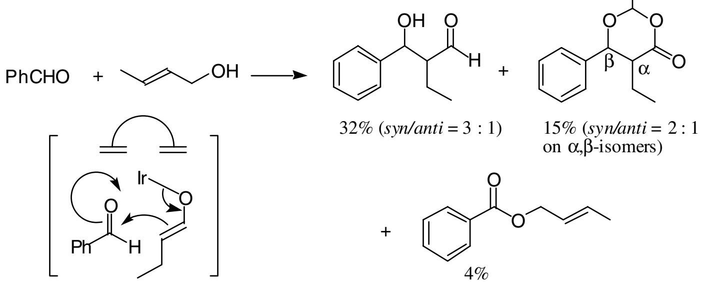
Entry	Aldehydes	Alcohols	% Yield of esters	
1			65	 (5 : 1)
2			71	 (5 : 1)
3			96	 (5 : 1)
4			87	
5			88	
6			90	 (4 : 1)
7			85	 (5[b] : 1)
8			76	 (5[b] : 1)
9			73	 (3 : 1)
10			85	 (3 : 1)
11			77	

[b] The esters are containing isomeric inner olefins.

[a] The reaction conditions of entry 3 in Table 1 were used.

iridium to form the resulting alkoxo complex and the outer-sphere attack of the pendant alkoxo moiety onto the coordinated aldehyde results in the subsequent C–O bond formation.

In addition, aromatic aldehyde showed a little bit different behavior in the reaction. The reaction of benzaldehyde with crotyl alcohol gave a small amount of the expected ester. The electron-attractive character of the aromatic moiety, compared to that of aliphatic one, might be suitable to undergo a tandem isomerization aldol reaction.[3] The major products in the reaction were composed of aldol products and their derivatives (Scheme 5). The derivatives are considered to result from the extended oxidative esterification of the aldol products and the following cyclization.



Scheme 5.

Acknowledgements

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References and notes

1. Davies, S. G. *Organotransition Metal Chemistry, Applications to Organic Synthesis*; Pergamon: Oxford, 1982, pp 282–290.
2. (a) Pannetier, G.; Bonnaire, R.; Fouqeroux, P. *J. Organometal. Chem.* **1971**, *30*, 411; (b) Baudry, D.; Ephritikhine, M.; Felkin, H. *Nouveau J. Chimie* **1977**, *2*, 355; (c) Ohmura, T.; Shirai, Y.; Yamamoto, Y.; Miyaura, N. *Chem. Commun.* **1998**, 1337.
3. Tandem isomerization aldol condensations using allylic alcohols: Fe: (a) Uma, R.; Gouault, N.; Crévisy, C.; Grée, R. *Tetrahedron Lett.* **2003**, *44*, 6187; (b) Crévisy, C.; Wietrich, M.; Le Boulaire, V.; Uma, R.; Grée, R. *Tetrahedron Lett.* **2001**, *42*, 395; Rh: (a) Gazzard, L. J.; Motherwell, W. B.; Sandham, D. A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 979; (b) Uma, R.; Davies, M.; Crévisy, C.; Grée, R. *Tetrahedron Lett.* **2001**, *42*, 3069.
4. A hydrido-π-allylic intermediate was also proposed: Bergens, S. H.; Bosnich, B. *J. Am. Chem. Soc.* **1991**, *113*, 958.
5. Bäckvall, J.-E.; Andresson, U. *Tetrahedron Lett.* **1993**, *34*, 5459.
6. (a) Fujita, K.; Furukawa, S.; Yamaguchi, R. *J. Organomet. Chem.* **2002**, *649*, 289; (b) Suzuki, T.; Morita, K.; Tsuchida, M.; Hiroi, K. *J. Org. Chem.* **2003**, *68*, 1601.
7. Blum, O.; Milstein, D. *J. Am. Chem. Soc.* **2002**, *124*, 11456.
8. Murahashi, S.; Naota, T.; Ito, K.; Maeda, Y.; Taki, H. *J. Org. Chem.* **1987**, *52*, 4319.
9. (a) Krug, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 1674; (b) Han, R.; Hillhouse, G. L. *J. Am. Chem. Soc.* **1997**, *119*, 8135.
10. Suzuki, T.; Morita, K.; Tsuchida, M.; Hiroi, K. *Org. Lett.* **2000**, *4*, 2361.
11. Martín, M.; Sola, E.; Torres, O.; Plou, P.; Oro, L. A. *Organometallics* **2003**, *22*, 5406.
12. General procedure for the oxidative esterification: To an oven-dried round bottomed flask were added $[IrCl(cod)]_2$ (33 mg, 0.05 mmol) and K_2CO_3 (14 mg, 0.1 mmol) in toluene (2 mL) under Ar. To this solution were slowly added aldehyde (1 mmol) and alcohol (2 mmol). The reaction mixture was stirred at rt for 12 h. The reaction was quenched with saturated NH_4Cl (5 mL). The organic layer was separated and the aqueous layer was extracted with ether (10 mL × 3). The combined organic layers were dried over anhydrous $MgSO_4$. After evaporation of the solvent, the crude residue was purified by flash column chromatography on silica gel to give the resulting esters.