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Oxidative dimerization of primary alcohols to esters catalyzed by iridium complexes

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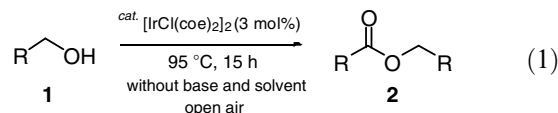
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Abstract—Primary alcohols undergo efficiently oxidative dimerization by iridium complexes under air without any solvent to form esters in fair to good yields. For instance, the reaction of 1-dodecanol in the presence of $[IrCl(coe)_2]_2$ (3 mol %) at 95 °C for 15 h produced dodecyl dodecanoate in 91% isolated yield. This is the first successful Ir-catalyzed oxidative dimerization of primary alcohols to esters using air as an oxidant. Various primary alcohols are converted to the corresponding esters in fair to good yields.
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The homogeneous catalytic transformation of primary alcohols to esters has been carried out using $Pd(OAc)_2$[1] and $Ru_3(CO)_{12}$[2] in the presence of bromobenzene and tolane, respectively. The first systematic study of the catalytic oxidative condensation of alcohols was made by Murahashi and co-workers using $RuH_2(PPh_3)_4$ as a catalyst.[3] Thereafter, Cho and co-workers reported the α-alkylation of ketones with alcohols by the same ruthenium complex in the presence of stoichiometric amounts of a hydrogen acceptor like 1-dodecene and a base like KOH using dioxane as a solvent.[4] In contrast to the Ru-catalyzed α-alkylation of ketones with alcohols which calls for the presence of a hydrogen acceptor and the use of dioxane as a solvent, the $[IrCl(cod)]_2$-catalyzed α-alkylation of ketones with alcohols was achieved without both a hydrogen acceptor and a solvent. This reaction provides a very convenient clean route to aliphatic ketones to which a carbonyl function can be introduced into the desired position by choosing ketones and alcohols employed.[5] This strategy has been extended to the reaction between secondary alcohols and primary alcohols leading to β-alkylated secondary alcohols.[6] Recently, we have found that Ir complexes like $[IrOH(cod)]_2$ in the presence of a small amount of KOH catalyze the Guerbet reaction of primary alcohols to higher molecular alcohols through the aldol condensation of the resulting aldehydes and the subsequent

hydrogenation, for example, 1-butanol to 2-ethyl-1-hexanol.[7] The achievement of the Ir-catalyzed Guerbet reaction of primary alcohols which involves the formation of aldehydes as a transient intermediate prompted us to design a reaction system for the oxidative transformation of primary alcohols to esters. Quite recently, it has been reported that the Cp*Ir aminoalkoxide complex promotes the oxidative dimerization of primary alcohols to esters in the presence of K_2CO_3 and excess ketone (2.7 equiv) like 2-butanone which serves as hydrogen acceptor.[8] In this letter, we wish to report the Ir-catalyzed oxidative dimerization of alcohols to esters using air as an oxidant without any solvent and base (Eq. 1).

$$ \overset{\underset{\textstyle 1}{}}{R\frown OH} \quad \xrightarrow[\substack{95\ ^\circ C,\ 15\ h \\ \text{without base and solvent} \\ \text{open air}}]{^{cat.}\ [IrCl(coe)_2]_2\,(3\ mol\%)} \quad \overset{\underset{\textstyle 2}{}}{R\overset{O}{\frown}O\frown R} \qquad (1) $$

The reaction of 1-octanol (**1a**) to octyl octanoate (**2a**) was chosen as a model reaction and carried out under the influence of several iridium complexes (Table 1).

The reaction afforded **2a** as a major product together with small amounts of octanal (**3**) and octanoic acid (**4**). Among the catalysts examined, $[IrCl(coe)_2]_2$ and $[IrCl(cod)]_2$ were found to be good catalysts for the transformation of **1a** to **2a** (entries 1 and 2). It is important to note that the Ir-catalyzed dimerization could be achieved using air as an oxidant without a solvent at

Table 1. Oxidative dimerization of 1-octanol (**1a**) to octyl octanoate (**2**) by Ir-catalyst under various conditions[a]

Entry	Catalyst	Conv. (%)	Yield[b] (%)
1	[IrCl(coe)$_2$]$_2$	99	82
2	[IrCl(cod)]$_2$	99	76
3	[IrOH(cod)]$_2$	66	22 (36)[c]
4	[Ir(coe)$_2$]$^+$BF$_4^-$	91	61
5	[Cp*IrCl$_2$]$_2$	27	3
6[d]	[IrCl(coe)$_2$]	91	58
7[e]	[IrCl(coe)$_2$]$_2$	39	0

[a] Compound **1a** (2 mmol) was reacted in the presence of Ir-catalyst (3 mol %) under open air at 95 °C for 15 h.
[b] GLC yields. The yields were determined based on the alcohol (**1a**) used.
[c] Yield of heptane.
[d] Toluene (1 mL) was used as solvent.
[e] The reaction was carried out under Ar.

relatively lower temperature, although the ruthenium-catalyzed reactions are carried out at higher temperature of 147 °C for Ru$_3$(CO)$_{12}$[2] and 180 °C for RuH$_2$(PPh$_3$)$_4$.[3] In addition, the Ir-catalyst was not deactivated by the water generated during the reaction course to promote smoothly the dimerization of **1a** to **2a**, since the in situ generated water is often responsible for prevention of the desired reaction and decomposition of the catalyst. The reaction by the [IrOH(cod)]$_2$ complex, which promotes efficiently the Guerbet reaction of primary alcohols,[7] gave **2** in low yield (22%), and a considerable amount of heptane (36%) was detected after the reaction. The formation of heptane can be explained by the following sequential reactions, that is, the hydrogenation of heptene derived from the decarbonylation of an acyl Ir-complex generated by the oxidative addition of octanal to an Ir-complex. The formation of heptane shows that **1a** is smoothly dehydrogenated to octanal by the [IrOH(cod)]$_2$ complex, but this Ir-complex would tend to induce decarbonylation rather than oxidative dimerization of the octanal and **1a** (entry 3). A cationic complex, [Ir(cod)$_2$]$^+$BF$_4^-$, indicated moderate activity to give **2** in 61% yield (entry 4). However, the [Cp*IrCl$_2$]$_2$ complex having excellent dehydrogenation ability for alcohols[9] was inert for the present reaction (entry 5). When toluene was used as a solvent, the yield of **2** was decreased to 58% (entry 6). It was found that the reaction did not take place under Ar atmosphere without air (entry 7), in contrast to the RuH$_2$(PPh$_3$)$_4$-catalyzed reaction where alcohols are converted into esters with the evolution of hydrogen.[3]

On the basis of these results, several primary alcohols were allowed to react in the presence of [IrCl(coe)$_2$]$_2$ under air at 95 °C for 15 h (Table 2). Higher alcohols were more selectively dimerized than lower carbon-numbered alcohols to give the corresponding esters in good yields. For example, 1-dodecanol (**1f**) was converted to dodecyl dodecanoate (**2f**) in 94% yield (entry 5). Branched primary alcohols like 2-ethylhexanol (**1g**) were also oxidatively dimerized to 2-ethylhexyl 2-ethylhexanoate (**2g**) in good yield (entry 6). Cyclohexylmethanol (**1j**) and 2-phenylethanol (**1k**) were also converted to the corresponding esters, **2j** and **2k**, respectively, in substantial yields (entries 9 and 10). On the other hand,

when phthalyl alcohol (**1l**) was employed as a substrate, the reaction afforded phthalide (**2l**) in low yield (10%). However, the reaction took place smoothly in the presence of Na$_2$CO$_3$ (5 mol %) and PPh$_3$ (10 mol %) in toluene to afford **2l** in 86% yield (entry 11).

The reaction is rationally explained by the following reaction pathway (Scheme 1). The reaction is initiated by the in situ generation of an Ir–dihydride complex[5,10] via hydrogen transfer from alcohols (**1**) to an Ir-complex, which affords aldehydes. Subsequent dehydro-

Table 2. Oxidative dimerization of primary alcohols (**1**) to esters (**2**) by Ir-catalyst[a]

Entry	Alcohol (**1**)	Conv. (%)	Ester (**2**)[b] (%)
1[c]	**1b**	97	50
2	**1c**	94	88
3	**1d**	>99	90 (86)
4	**1e**	99	76
5	**1f**	99	94 (91)
6[d]	**1g**	98	80 (68)
7[e]	**1h**	98	51
8[d,e]	**1i**	97	56
9	**1j**	99	76
10	**1k**	82	61
11	**1l**	>99	86[f]

[a] Alcohol (2 mmol) was reacted in the presence of [IrCl(coe)$_2$]$_2$ (3 mol %) under open air at 95 °C for 15 h.
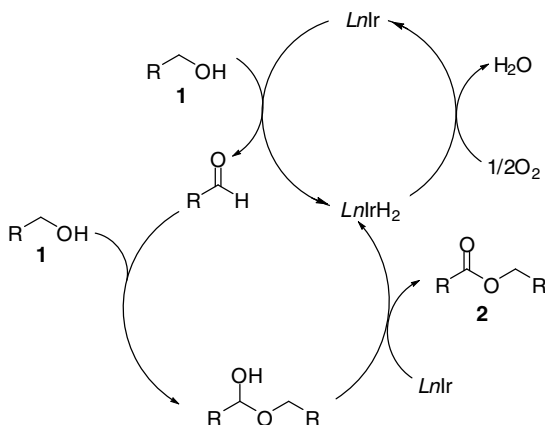[b] GLC yields. The numbers in parentheses show isolated yields. The yields were determined based on the alcohol (**1**) used.
[c] Toluene (0.1 mL) was used as solvent.
[d] The stereochemistry is not determined.
[e] Reaction time was 20 h.
[f] The reaction was performed in the presence of Na$_2$CO$_3$ (5 mol %), PPh$_3$ (10 mol %), and toluene (1 mL).

Scheme 1. A possible reaction pathway for the Ir-catalyzed reaction of **1** to **2**.

genation of hemiacetals derived from alcohols and the aldehydes by the action of the Ir-complex affords esters (**2**) and the Ir–dihydride complex. Then the Ir–dihydride complex reacts with dioxygen in air to liberate water as a by-product. In a previous paper, we reported that Cp_2ZrH_2 catalyzes efficiently the Tishchenko reaction of aldehydes to esters through an alkoxyzirconium species but not hemiacetal.[11] However, it is thought that the present reaction passes through the formation of hemi-acetal as a transient intermediate. This is supported by the fact that the $[IrCl(coe)_2]_2$ complex did not catalyze the Tishchenko reaction of aldehydes alone in the absence of alcohols under these conditions. A similar reaction pathway is also shown by Suzuki et al.[8]

In conclusion, we have found that primary alcohols undergo oxidative dimerization in the presence of a catalytic amount of $[IrCl(coe)_2]_2$ under air without any additive and solvent to give the corresponding esters in good yields. This method provides an environmentally clean route to esters from primary alcohols and air not using a base and a hydrogen acceptor like ketones.

General procedure for reaction of **1** *(Table 1, entry 1):* A mixture of **1a** (2 mmol) and $[IrCl(coe)_2]_2$ (0.06 mmol) was stirred at 95 °C for 15 h under open air. The product was isolated by column chromatography (230–400 mesh silica gel, *n*-hexane–ethyl acetate = 10:1).

The conversions and yields of products were estimated from the peak areas based on the internal standard technique using GLC. The products **2a**–**b**,[3a] **2c**,[12] **2d**,[3a] **2e**,[13] **2f**,[14] **2g**,[15] **2h**–**k**,[3a] and **2l**[16] were reported previously.

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