The Direct Conversion of Ethanol to Ethyl and Methyl Acetates Catalyzed by Iridium Complex

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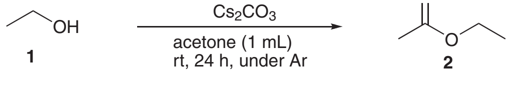
Ethanol was efficiently converted to ethyl and methyl acetates by $[Cp^*IrCl_2]_2$ combined with 2-(methylamino)ethanol and a base like Cs_2CO_3 at room temperature in acetone in high yield, which provides the first Ir-catalyzed direct route to ethyl and methyl acetates from ethanol.

Ethyl acetate is a very important feedstock, in particular as a solvent in painting and adhesive industries as well as the food industry.[1] Currently, ethyl acetate is manufactured industrially in the following three ways: the Fischer esterification of acetic acid with ethanol,[2] the Tishchenko reaction of acetaldehyde,[3] and the addition of acetic acid to ethylene.[4] An attractive strategic approach for the production of ethyl acetate is the direct synthesis from ethanol through a catalytic process. The homogeneous catalytic transformation of primary alcohols to esters has been examined using $Pd(OAc)_2$[5] and $Ru_3(CO)_{12}$.[6] A systematic study of the catalytic oxidative condensation of alcohols was made by Murahashi et al. using $RuH_2(PPh_3)_4$ catalyst.[7] In recent years, we[8] and other groups[9] have reported Ir-catalyzed alkylations using alcohols as alkylating agents. In addition, Ir-complexes like $[IrOH(cod)]_2$ combined with KOH catalyze the Guerbet reaction of primary alcohols to higher molecular alcohols.[10] In a previous paper, we reported the Ir-catalyzed aerobic oxidative esterification of primary alcohols to esters.[11] Unfortunately, lower alcohols like ethanol and propanol were difficult to convert to esters by this existing catalytic system.

On the other hand, Suzuki et al.[12] and Williams et al.[13] reported the dimerization of primary alcohols to esters by Cp*Ir-complex bearing an aminoalkoxy group and by $Ru(PPh_3)_3(CO)H_2$ with xantphos in the presence of a hydrogen acceptor like 2-butanone and crotononitrile, respectively. However, there is no report of the direct conversion of ethanol to ethyl acetate, which is thought to be the most important transformation as a practical industrial method. In this paper, we wish to report oxidative dimerization of ethanol (**1**) to ethyl acetate (**2**) and methyl acetate (**5**) using acetone as a hydrogen acceptor by using easily accesible Ir-catalyst which is generated in situ by adding 2-(methylamino)-ethanol to $[Cp^*IrCl_2]_2$ (eq 1).

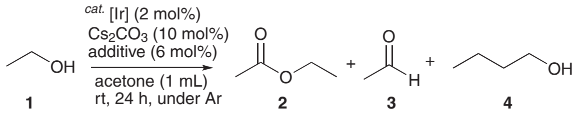
Compound **1** was allowed to react under the influence of several Ir-complexes and Cs_2CO_3 as a base using acetone as a hydrogen acceptor at room temperature (Table 1).[14]



(1)

The reaction was first examined by using $[IrCl(coe)_2]_2$ and $[IrCl(cod)]_2$, which are efficient catalysts for the oxidative dimerization of 1-butanol to 2-ethyl-1-hexanol,[11] but these Ir-complexes were found to be poor catalysts for the conversion of **1** to **2** (Entries 1 and 2). $[IrOH(cod)]_2$ promoted the oxidative dimerization of **1** to **2** in moderate yield (42%) along with a small amount of 1-butanol (**4**) (Entry 3).[15] $[Cp^*IrCl_2]_2$ was also inefficient to afford **2** (7%) and acetaldehyde (**3**) (8%) (Entry 4). It is reported that the dehydrogenation of secondary alcohols to ketones by $[Cp^*IrCl_2]_2$ is accelerated by adding 2-hydroxypyridine.[16] However, the addition of 2-hydroxypyridine was sluggish for the reaction with primary alcohol like ethanol and the yield of **2** was very low (Entries 5 and 6).

Table 1. Oxidative dimerization of ethanol (**1**) to ethyl acetate (**2**) by Ir-complex under various reaction conditions[a]



Entry	Ir-complex	Additive	Conv. /%	Yield/%[b]		
				2	**3**	**4**
1	$[IrCl(coe)_2]_2$	—	18	6(33)	3	—
2	$[IrCl(cod)]_2$	—	20	6(30)	3	—
3	$[Ir(OH)(cod)]_2$	—	61	42(69)	—	2
4	$[Cp^*IrCl_2]_2$	—	30	7(23)	8	—
5	$[Cp^*IrCl_2]_2$	2-Hydroxypyridine	12	5(42)	3	—
6[c]	$[Cp^*IrCl_2]_2$	2-Hydroxypyridine	6	3(50)	—	—
7	$[Cp^*IrCl_2]_2$	$MeNH(CH_2)_2OH$	89	85(96)	—	3
8[d]	$[Cp^*IrCl_2]_2$	$MeNH(CH_2)_2OH$	78	68(87)	—	2
9	$[IrCl(coe)_2]_2$	$MeNH(CH_2)_2OH$	12	5(42)	3	—
10	$[IrCl(cod)]_2$	$MeNH(CH_2)_2OH$	15	—	6	—
11	$[Ir(OH)(cod)]_2$	$MeNH(CH_2)_2OH$	59	41(69)	—	2

[a]See Ref. 14. [b]Determined by GC. Numbers in parentheses show selectivity [(yield of **2**)/(conversion of **1**)]. [c]Reaction was performed in the absence of acetone. [d]Ir-complex (1 mol %) was used.

Fortunately, the reaction was found to be efficiently promoted by adding a catalytic amount of 2-(methylamino)ethanol to the $[Cp^*IrCl_2]_2$ to give **2** in good yield (85%) even at room temperature (Entry 7). This is the first successful direct conversion of **1** to **2** in high yield. However, no such positive effects of 2-(methylamino)ethanol were observed by the reaction using $[IrCl(coe)_2]_2$, $[IrCl(cod)]_2$, and $[IrOH(cod)]_2$ as catalysts (Entries 9–11). Another important feature of the present reaction is that the liberated hydrogen from **1** can be stored by acetone as a form of 2-propanol, which is widely used as an important raw material in chemical industry.

Furthermore, we performed the reaction on multigram scale of **1** (2 g) by using a lower amount of $[Cp^*IrCl_2]_2$ (0.5 mol %), 2-(methylamino)ethanol (1 mol %), Cs_2CO_3 (3 mol %) in acetone (5.5 mL) under these reaction conditions at rt for 48 h, and **2** was obtained in high yield (1.53 g, 80%).

The reaction of **1** catalyzed by $[Cp^*IrCl_2]_2$ was examined by adding several analogues (Table 2). Like 2-(methylamino)ethanol, 2-(ethylamino)ethanol promoted efficiently the dimerization of **1** to **2** in 83% yield (Entry 1). However, the yield of **2** was decreased

Table 2. Effect of additives and bases in the Ir-catalyzed oxidative dimerization of ethanol (**1**) to ethyl acetate (**2**)[a]

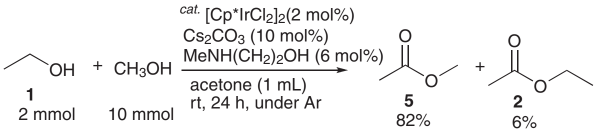
Entry	Additive	Base	Conv. /%[b]	Yield/%[b] **2**	**3**	**4**
1	$EtNH(CH_2)_2OH$	Cs_2CO_3	86	83(97)	—	4
2	*n*-$PrNH(CH_2)_2OH$	Cs_2CO_3	83	73(88)	—	2
3	*n*-$BuNH(CH_2)_2OH$	Cs_2CO_3	55	48(87)	—	—
4	$PhNHC_2H_4OH$	Cs_2CO_3	25	6(24)	—	—
5	$H_2NC_2H_4OH$	Cs_2CO_3	32	16(50)	8	—
6	$H_2NC_2H_4NH_2$	Cs_2CO_3		No reaction		
7	$MeNH(CH_2)_2OH$	Na_2CO_3	27	2(7)	2	—
8	$MeNH(CH_2)_2OH$	K_2CO_3	45	29(64)	4	—
9	$MeNH(CH_2)_2OH$	KOH	67	57(85)	—	—
10	$MeNH(CH_2)_2OH$	—	5	—	—	—
11[c]	$MeNH(CH_2)_2OH$	K_2CO_3	85	81(95)	2	—
12[d]	$MeNH(CH_2)_2OH$	Cs_2CO_3	95	81(85)	—	—
13[e]	$MeNH(CH_2)_2OH$	Cs_2CO_3	95	84(88)	—	—
14[f]	$MeNH(CH_2)_2OH$	Cs_2CO_3	82	56(68)	—	—
15[g]	$MeNH(CH_2)_2OH$	Cs_2CO_3	28	5(18)	—	—
16[h]	$MeNH(CH_2)_2OH$	Cs_2CO_3	11	3(27)	—	—
17[i]	$H_2NC(Ph)_2CH_2OH$	K_2CO_3	88	82(93)	—	—

[a]See Ref. 14. [b]Determined by GC. Numbers in parentheses show selectivity [(yield of **2**)/(conversion of **1**)]. [c]K_2CO_3 (30 mol %) was used. [d]2-Butanone (1 mL, 11.2 mmol) was used in place of acetone. [e]2-Pentanone (1 mL, 9.4 mmol) was used in place of acetone. [f]Acetophenone (1 mL, 8.6 mmol) was used in place of acetone. [g]1-Octene (1 mL, 6.4 mmol) was used in place of acetone. [h]1,7-Octadiene (1 mL, 6.7 mmol) was used in place of acetone. [i]$H_2NC(Ph)_2CH_2OH$ (4 mol %) and K_2CO_3 (30 mol %) were used.

with increasing the carbon number of the alkyl group on the amino group (Entries 2 and 3), while the reaction was not accelerated by the addition of 2-anilinoethanol or 2-aminoethanol (Entries 4 and 5). 1,2-Ethylenediamine was found to entirely inhibit the present reaction (Entry 6). The choice of base is an important factor to promote the reaction. As for a base in the present reaction, Cs_2CO_3 gave the best result, but Na_2CO_3, K_2CO_3, or KOH resulted in considerable decrease of the conversion of **1** (Entries 7–9). Needless to say, no reaction was induced in the absence of a base (Entry 10). When 30 mol % of K_2CO_3 was employed under these conditions, **2** was obtained in 81% yield (Entry 11). The reaction was also performed by the use of 2-butanone or 2-pentanone, but acetophenone was less efficient hydrogen acceptor (Entries 12–14). The use of 1-octene or 1,7-octadiene as a hydrogen acceptor brought about unsatisfactory results (Entries 15 and 16).

Suzuki reported that the $Cp^*Ir[OCH_2C(Ph)_2NH]$ shows the efficient catalytic activity for the direct conversion of alcohols to esters.[12] Thus, $H_2NC(Ph)_2CH_2OH$ prepared independently and K_2CO_3 were used as additives, and the reaction was found to give the comparable result to our system (Entry 17). This result suggests that a similar aminoalkoxy-substituted Ir-complex would be formed in our catalytic system.

This method is applicable to the methyl esterification of ethanol using methanol. Under the optimized conditions as showed in Entry 7, Table 1, ethanol **1** was reacted in the presence of methanol (5 equiv) to afford methyl acetate (**5**) in high yield (82%) and selectivity (93%) (eq 2).



(2)

The present transformation of **1** to **2** is considered to proceed in a similar reaction pathway shown by previous reports.[11,12] The reaction is initiated by the in situ generation of an Ir–dihydride complex[8,9,11] via hydrogen transfer from **1** to an Ir-complex, which affords acetaldehyde (**3**). Subsequent hemiacetal formation from **1** and **3** followed by dehydrogenation by the action of Ir-complex affords **2**, and then the hydrogen transfer from the resulting Ir–dihydride complex to acetone to regenerate 2-propanol and an Ir-complex. A real active species seems to be an Ir-complex derived from $[Cp^*IrCl_2]_2$ and 2-(methylamino)ethanol. However, all attempts to isolate an active Ir-complex were unsuccessful at present stage.

In conclusion, ethanol (**1**) was efficiently converted into ethyl acetate (**2**) and methyl acetate (**5**) in the presence of methanol by using a $[Cp^*IrCl_2]_2$ combined with 2-(methylamino)ethanol as catalyst. Further study of the characterization of the active catalyst species and detailed elucidation of the reaction mechanism is currently under investigation.

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14 Typical reaction procedure (Table 1, Entry 7): A mixture of **1** (2 mmol, 92 mg) and acetone (1 mL, 13.6 mmol) in the presence of $[Cp^*IrCl_2]_2$ (2 mol %, 0.04 mmol, 32 mg), 2-(methylamino)ethanol (6 mol %, 0.12 mmol, 9 mg), and Cs_2CO_3 (10 mol %, 0.2 mmol, 65 mg) was stirred at room temperature for 24 h under Ar.

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