An efficient ligand-free method for the transfer hydrogenation of ketones and aldehydes catalyzed by different complexes

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Abstract: A very efficient ligand-free method was developed for the transfer hydrogenation of ketones and aldehydes catalyzed by different metal complexes. With this catalytic system, the catalytic performance and catalytic stability of different Ir, Ru, and Pd complexes were more favorable than those of the previously reported systems for transfer hydrogenation. This ligand-free catalytic system showed good stability and excellent activity even with lower catalyst concentrations for the ketones and aldehydes tested.

Key words: Transfer hydrogenation, ruthenium, iridium, palladium, ketone, aldehyde

1. Introduction

Transfer hydrogenation is an effective method for the reduction of ketones and aldehydes to alcohols under mild reaction conditions.[1−16] Catalytic reduction of ketones to alcohols is significant because the products are vitally important for many industries.[17] Transfer hydrogenation can be regarded in the field of green chemistry thanks to its economical and environmentally friendly reaction. Avoiding the use of H_2 pressure or hazardous reducing agents by using nontoxic hydrogen donors such as alcohols makes it an indispensable method.[18] So far, different metals such as platinum,[19] gold,[20] iridium,[21] rhodium,[22] and ruthenium[23] have been used as catalyst for catalytic reduction of ketones. The most active and selective hydrogen transfer catalysts are iridium, ruthenium, and rhodium complexes bearing phosphine and NHC ligands.[1−6] Noyori's ruthenium catalysts with chiral tetradentate ligands and arene complexes based on chiral β-amino alcohol or N-tosylethylenediamine ligands that operate through a bifunctional metal ligand mechanism are also well known.[24] Previous studies showed that iridium-NHC complexes are more active than their Rh-NHC analogues and a number of highly efficient iridium catalysts have been reported.[25,26] However, metal-based catalyst systems are expensive because synthesis of metal complexes requires many chemical synthetic steps. Hence, there is a need for a cheap and as green as possible catalytic system capable of showing the same catalytic activities of transition as metal complex-based systems. Further research might seek to develop a cheaper and simpler and an atom-efficient catalyst system.

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2. Experimental

Unless otherwise stated, all reactions for transfer hydrogenation were carried out under argon in flame-dried glassware using standard Schlenk techniques. The solvents used were purified by distillation over the drying agents indicated and were transferred under Ar:Et$_2$O (Na/K alloy) and 2-propanol (CaH$_2$). Melting points were determined in glass capillaries under air with an Electrothermal-9200 melting point apparatus. All starting materials were commercially available and used without any purification. ^{1}H and ^{13}C NMR were measured at 400 MHz and 100 MHz in CDCl$_3$ with Me$_4$Si as an internal standard. Yields and substrate identities were determined by GC analysis of the reaction mixture using a Shimadzu GC 2010-Plus GC-FID system. Column: TeknokromaTRB-5 capillary column, 30 m × 0.32 mm × 0.25 μm. Oven program used: initial temperature at 50 °C, held for 1 min, ramped 2 °C/min to 90 °C, held for 3 min, ramp 40 °C/min to 240 °C, held for 10 min. The temperatures of the injector and detector were held at 240 °C.

A typical catalytic reduction procedure for ketones and aldehydes is as follows:

Catalyst (0.75 mol%), KOH (4 mmol), ketone (1 mmol), and 5 mL of 2-propanol were added to a Schlenk flask under argon atmosphere. The reaction mixture was stirred at 80 °C for 30 min. Cold reaction mixture was passed through silica gel. The conversions and yields of products were estimated from the peak areas based on the internal standard technique using GC. All of the obtained products were reported previously.

3. Results and discussion

So far, ketones and aldehydes have been reduced to alcohol with metal complexes bearing different ligands.[1−16,24−26] The disadvantages of metal-based catalyst systems include the cost and toxicity of these precious metals and ligands. Environmental concerns have directed research to find mild technologies and environmentally friendly catalysts and catalytic systems. Even though there are some applications on hydrogen transfer reactions with metal-free catalytic systems,[27−29] metal-free catalyst systems cannot compete in terms of efficiency and time with metal-based systems.[27−29] Hence, we present a ligand-free method that allows hydrogen transfer of different ketones and aldehydes in moderate conditions and in the presence of catalytic amounts of simple and cheap metal complexes (Figure 1). Moreover, this ligand-free method provided an efficient atom reaction with economic and environmental advantages without any waste. Our method is totally simple, very effective, and most importantly ligand-free.

To determine optimum reaction conditions, the reaction of p-chloroacetophenone with [IrCl(COD)]$_2$ was chosen as a model reaction and was carried out under various reaction conditions. p-Chloroacetophenone (1
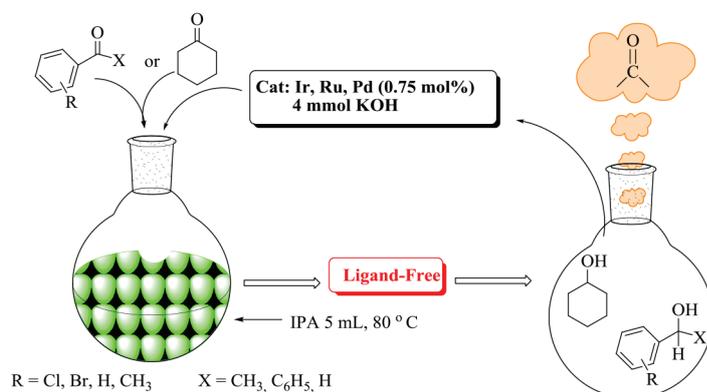

Figure 1. Transfer hydrogenation of ketones and aldehydes under ligand-free catalytic conditions.

Table 1. Transfer hydrogenation of ketones and aldehydes catalyzed by Ir, Ru, and Pd complex derivatives.

Entry	Catalyst	Substrate	[a]Conversion %
1	[IrCl(COD)]$_2$	p-Chloroacetophenone	96[b]
2	[RuCl$_2$(p-cymene)]$_2$	p-Chloroacetophenone	65[b]
3	Pd(OAc)$_2$	p-Chloroacetophenone	47[b]
4	[IrCl(COD)]$_2$	p-Chloroacetophenone	99[c]
5	[IrCl(COD)]$_2$	p-Chloroacetophenone	43[h]
6	[IrCl(COD)]$_2$	p-Chloroacetophenone	98[i]
7	[IrCl(COD)]$_2$	p-Chloroacetophenone	1[d]
8	[RuCl$_2$(p-cymene)]$_2$	p-Chloroacetophenone	99
9	[RuCl$_2$(p-cymene)]$_2$	p-Chloroacetophenone	65[c]
10	[RuCl$_2$(p-cymene)]$_2$	p-Chloroacetophenone	84[i]
11	[RuCl$_2$(p-cymene)]$_2$	p-Chloroacetophenone	1[d]
12	Pd(OAc)$_2$	p-Chloroacetophenone	74
13	[IrCl(COD)]$_2$	Acetophenone	55
14	[RuCl$_2$(p-cymene)]$_2$	Acetophenone	37
15	Pd(OAc)$_2$	Acetophenone	32
16	[IrCl(COD)]$_2$	Cyclohexanone	95
17	[RuCl$_2$(p-cymene)]$_2$	Cyclohexanone	100
18	Pd(OAc)$_2$	Cyclohexanone	70
19	[IrCl(COD)]$_2$	p-Chlorobenzaldehyde	100
20	[RuCl$_2$(p-cymene)]$_2$	p-Chlorobenzaldehyde	100
21	Pd(OAc)$_2$	p-Chlorobenzaldehyde	100
22	[IrCl(COD)]$_2$	p-Bromoacetophenone	36[e]/12[f]/52
23	[RuCl$_2$(p-cymene)]$_2$	p-Bromoacetophenone	26[e]/1[f]/73
24	Pd(OAc)$_2$	p-Bromoacetophenone	14[e]/86[f]
25	No metal	4-Chloroacetophenone	31[g]
26	No metal	Acetophenone	10[g]
27	No metal	Cyclohexanone	30[g]
28	No metal	p-Chloroacetophenone	90[j]
29	No metal	p-Chloroacetophenone	35[k]
30	PdCl$_2$	p-Chloroacetophenone	64
31	IrCl$_3$.nH$_2$O	p-Chloroacetophenone	98
32	RuCl$_3$.xH$_2$O	p-Chloroacetophenone	72
33	IrCl$_3$.nH$_2$O	Acetophenone	45
34	RuCl$_3$.xH$_2$O	Acetophenone	25
35	PdCl$_2$	Acetophenone	15
36	IrCl$_3$.nH$_2$O	Cyclohexanone	89
37	RuCl$_3$.xH$_2$O	Cyclohexanone	90
38	PdCl$_2$	Cyclohexanone	63
39	Pd(PPh$_3$)$_2$(OAc)$_2$	p-Chloroacetophenone	41[f]/59[e]
40	[IrCl(COD)]$_2$	p-Chloroacetophenone	0[l]
41	[IrCl(COD)]$_2$	p-Chloroacetophenone	98[m]
42	[IrCl(COD)]$_2$	p-Chloroacetophenone	87[n]
43	[IrCl(COD)]$_2$	p-Chloroacetophenone	66[o]

[a] Reaction conditions: 1.0 mmol substrate, i-PrOH (5 mL), KOH (4 mmol), Ir, Ru, Pd (0.75 mol%), 80 °C, 30 min. Purity of compounds is checked by GC and GC-MS and yields are based on ketones. Yields were determined by GC. [b] Reaction time 10 min. [c] Cat.Con. 0.0025 mol%. [d] At room temperature. [e] 1-Phenylethanol as side product. [f] Acetophenone as side product. [g] No metal. [h] K$_2$CO$_3$ as a base. [i] Reaction temperature 50 °C. [j] Reaction time 3 h. [k] Reaction time 1 h. [l] No base. [m] Cat.Con. 0.1 mol%. [n] Cat.Con. 0.05 mol%. [o] Cat.Con. 0.0025 mol%.

mmol) was catalyzed by $[Ir(COD)Cl]_2$ (0.75 mol%) in the presence of KOH (4 mmol) and 5 mL of 2-propanol at 80 °C over 10 min (Table 1, entry 1). With the same catalytic conditions, p-chloroacetophenone substrate was catalyzed by $[RuCl_2(p\text{-cymene})]_2$ and $Pd(OAc)_2$ metal complexes with lower ratios (Table 1, entry 2, 3). The classical efficient transfer hydrogenation of ketones and aldehydes was achieved under the influence of different alkali bases such as $KOBu^t$, KOH, and K_2CO_3. As in the literature,[30] no conversion to the product was observed in the absence of base (Table 1, entry 40). K_2CO_3, KOH, and $KOBu^t$ were tried as different bases with the $[Ir(COD)Cl]_2/p$-chloroacetophenone catalytic system. We observed that KOH and $KOBu^t$ showed good conversions when compared to K_2CO_3 in the transfer hydrogenation reactions (Table 1, entry 5). By using a stronger base, a higher conversion rate was observed. K_2CO_3 (23%) < NaOH(90%) < KOH(100%) = ^{t}-BuOK (100%). Transfer hydrogenation of p-chloroacetophenone was examined in the absence of KOH in 2-propanol. The $[Ir(COD)Cl]_2$/KOH catalyst/base pair is the best compromise between optimum reaction rate in 2-propanol because the reactions that were examined without metal complex and/or base were not satisfactory in terms of efficiency or reaction time (Table 1, entry 25–29, 40).

The performances of Ir, Ru, and Pd complexes were also tested using a variety of substrates (Table 1). With 0.75 mol% catalyst loading, the $[IrCl(COD)]_2$ complex gave very high conversions in 10 min for most binding of the substrates tested. In addition, lower catalyst concentration (0.25 mol%) (Table 1, entry 4, 9) and lower temperature conditions (Table 1, entry 6, 10) for $[IrCl(COD)]_2$ and $[RuCl_2(p\text{-cymene})]_2$ complexes were also investigated. All the results indicate that $[IrCl(COD)]_2$ showed a better performance than the other catalysts at every turn with the substrates tested.

Determining the rate of conversion of substrate to product over time by catalysts was another aim of our work. Plots of conversion versus time for $[IrCl(COD)]_2$ (0.25 mol%) and $[RuCl_2(p\text{-cymene})]_2$ (0.25 mol%) complexes were investigated with p-chloroacetophenone and the results are summarized in Table 2 and Figure 2. Reactions were monitored by taking aliquots from the reaction mixture at set intervals and the percentage conversions were determined. It is very clear that the activity of $[IrCl(COD)]_2$ complex is double that of $[RuCl_2(p\text{-cymene})]_2$ complex under the same reaction conditions. The reduction in catalyst performance of $[RuCl_2(p\text{-cymene})]_2$ complex over time is drastic. We think that this occurred due to decreasing concentration of the $[RuCl_2(p\text{-cymene})]_2$ and stopping the reaction every 5 min. Despite all these difficulties, the catalytic performance of $[IrCl(COD)]_2$ was excellent even at lower concentration (Table 1, entry 42, 43). This excellent performance can be attributed to the nature of the Ir metal center.
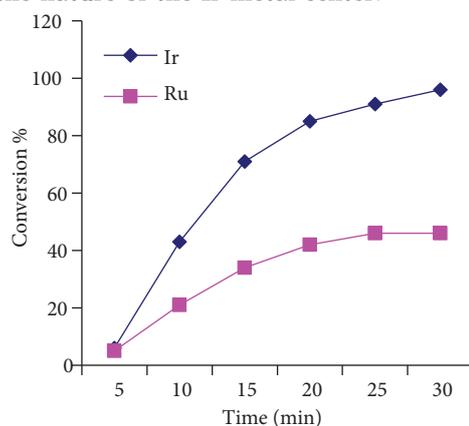

Figure 2. Plot of conversion vs. time for p-chloroacetophenone (1 mmol) catalyzed by $[IrCl(COD)]_2$ (0.25 mol%) and $[RuCl_2(p\text{-cymene})]_2$ (0.25 mol%).

Table 2. Transfer hydrogenation of p-chloroacetophenone catalyzed by [IrCl(COD)]$_2$ (0.25 mol%) and [RuCl$_2$(p-cymene)]$_2$ at 0.25 mol% concentration.

Entry	Catalyst	Time (min)	[a]Conversion %
1	[IrCl(COD)]$_2$	5	6
2	[IrCl(COD)]$_2$	10	43
3	[IrCl(COD)]$_2$	15	71
4	[IrCl(COD)]$_2$	20	85
5	[IrCl(COD)]$_2$	25	91
6	[IrCl(COD)]$_2$	30	96
7	[RuCl$_2$(p-cymene)]$_2$	5	5
8	[RuCl$_2$(p-cymene)]$_2$	10	21
9	[RuCl$_2$(p-cymene)]$_2$	15	34
10	[RuCl$_2$(p-cymene)]$_2$	20	42
11	[RuCl$_2$(p-cymene)]$_2$	25	46
12	[RuCl$_2$(p-cymene)]$_2$	30	46

[a] Reaction conditions: 1.0 mmol p-chloroacetophenone, i-PrOH (5 mL), KOH (4 mmol), [IrCl(COD)]$_2$, and [RuCl$_2$(p-cymene)]$_2$ (0.25 mol%), 80 °C, 30 min. Purity of compounds is checked by GC and GC-MS and conversions are based on ketones. Conversions were determined by GC.

To determine the stability of this catalyst system, [IrCl(COD)]$_2$ (0.75 mol%) was tested under normal operating conditions. However, after 20 min (100% conversion) an additional 1 mmol of p-chloroacetophenone was added and the reaction was monitored, and then after 70 min a third aliquot of substrate was added. After the third substrate addition, [IrCl(COD)]$_2$ catalyst was still stable and active (Figure 3). When we used p-bromoacetophenone as a substrate, we observed some acetophenone and 1-phenylethanol as side products (Table 1, entry 22–24). We think that these side products were produced by the strong base because bromine can be removed easily under strong basic conditions. When p-chloroacetophenone was used as substrate, side products were not observed with [IrCl(COD)]$_2$, [RuCl$_2$(p-cymene)]$_2$, or Pd(OAc)$_2$ due to the nature of the strong chlorine bond. Side products were observed just with Pd(PPh$_3$)$_2$(OAc)$_2$ catalysts (Table 1, entry 39). However, the side product that appeared from different substrates was catalyzed successfully to corresponding alcohol by catalysts. Reduction of aromatic aldehydes and ketones to alcohol with this catalytic system is indisputable.
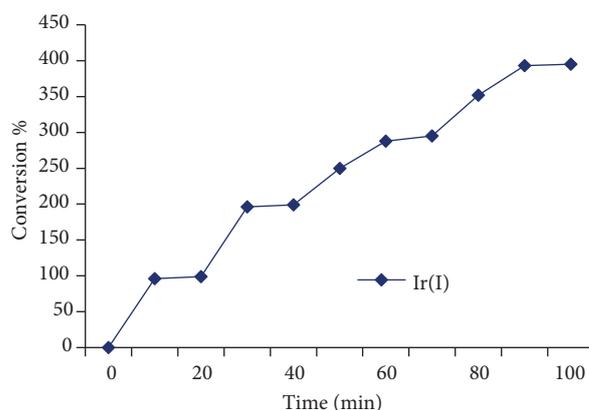
Figure 3. Lifetime studies for catalyst [IrCl(COD)]$_2$ (0.75 mol%) with p-chloroacetophenone as substrate (1 mmol).

In conclusion, the above results with different metals and substrates show that transfer hydrogenation reactions of ketones and aldehydes can easily be done under ligand-free and mild circumstances even at lower concentrations. The ligand-free catalytic system has some positive aspects and is preferable to the ligand-using systems and the metal-free systems.

Acknowledgment

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