Iridium-Catalyzed Transfer Hydrogenation of α,*β*-Unsaturated and Saturated Carbonyl Compounds with 2-Propanol

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Received April 6, 2001

The selective transfer hydrogenation of α,*β*-unsaturated carbonyl compounds to saturated ones was achieved by the use of 2-propanol as a hydrogen donor under the influence of catalytic amounts of [Ir(cod)Cl]$_2$, 1,3-bis(diphenylphosphino)propane (dppp), and Cs_2CO_3. Thus, a variety of conjugated enones were allowed to react with 2-propanol in the presence of the [Ir(cod)Cl]$_2$/dppp/Cs_2CO_3 system to give the corresponding saturated carbonyl compounds in good to excellent yields without formation of allylic alcohols. Both dppp and Cs_2CO_3 were essential components to achieve the reduction satisfactorily. Additionally, the reduction of carbonyl compounds to alcohols was also promoted by the same catalytic system. When the reaction of a 1:1 mixture of a conjugated ketone and a saturated ketone with 2-propanol was carried out in the presence of [Ir(cod)Cl]$_2$ combined with dppp and Cs_2CO_3, the reduction of the α,*β*-unsaturated ketone was found to take place in preference to that of the saturated ketone.

Introduction

Chemoselective reduction of α,*β*-unsaturated carbonyl compounds using an alcohol as a hydrogen source has been widely studied, since the reaction is easily carried out under mild conditions using an environmentally benign and safe reagent like 2-propanol. The selective reduction of the carbonyl group of α,*β*-unsaturated compounds to allylic alcohols has been achieved with relative ease.[1,2] In contrast, the transfer hydrogenation of the alkenic double bond of conjugated enones is limited.[3] The transfer hydrogenation of conjugated enones with an alcohol is performed by the use of ruthenium[1a−c,4] or rhodium[5] complexes as catalyst, but the reduction using iridium complexes is rare.[2] Here, we wish to report the Ir complex-catalyzed selective transfer hydrogenation of α,*β*-unsaturated carbonyl compounds to saturated ones and the reduction of carbonyl compounds using 2-propanol as a hydrogen donor.

Table 1. Transfer Hydrogenation of 4-Phenyl-3-buten-2-one (1) to 4-Phenylbutan-2-one (2) Catalyzed by [Ir(cod)Cl]$_2$ under Selected Conditions[a]

entry	phosphine	base	convn (%)	yield (%)
1[b]	PCy_3	Cs_2CO_3	76	58
2[b]	PPh_3	Cs_2CO_3	99	37[c]
3	dppe	Cs_2CO_3	89	88
4	dppp	Cs_2CO_3	93	93
5	dppb	Cs_2CO_3	93	87
6			2	1
7	dppp		31	20
8		Cs_2CO_3	42	35
9	dppp	Na_2CO_3	58	52
10	dppp	Et_3N	25	20

[a] Compound **1** (0.5 mmol) was allowed to react with 2-propanol (5 mmol) in the presence of a catalytic amount of [Ir(cod)Cl]$_2$ (2 mol %), phosphine (2 mol %), and base (2 mol %) in toluene (0.5 mL) at 80 °C for 4 h. [b] Phosphine (4 mol %) was used. [c] 4-Phenyl-2-butanol (60%) was also obtained.

Previously, we have shown the conversion of allyl homoallyl ethers to *γ*,*δ*-unsaturated carbonyl compounds through double-bond migration followed by the Claisen rearrangement by the use of a system consisting of [Ir(cod)Cl]$_2$/PCy_3/Cs_2CO_3.[6] In the course of the study on the behavior of the catalyst, we have found that the [Ir(cod)Cl]$_2$/phosphine/Cs_2CO_3 system serves as an efficient catalyst for the reduction of α,*β*-unsaturated carbonyl compounds as well as carbonyl compounds using 2-propanol as a hydrogen source.

Results

Table 1 shows the representative results for the transfer hydrogenation of 4-phenyl-3-buten-2-one (**1**) with 2-propanol under selected conditions (eq 1). Treatment of **1** with 2-propanol under the influence of catalytic amounts of [Ir(cod)Cl]$_2$, PCy_3, and Cs_2CO_3 at 80 °C for 4 h gave 4-phenylbutan-2-one (**2**) in 58% yield (Table 1, entry 1). The reaction was found to be considerably

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(1) (a) Mizugaki, T.; Kanayama, Y.; Ebitani, K.; Kaneda, K. *J. Org. Chem.* **1998**, *63*, 2378. (b) Bianchini, C.; Peruzzini, M.; Farnetti, E.; Kašper, J.; Graziani, M. *J. Organomet. Chem.* **1995**, *488*, 91. (c) Bhaduri, S.; Sharma, K. *J. Chem. Soc., Chem. Commun.* **1988,** 173. (d) Yoshinaga, K.; Kito, T.; Ohkubo, K. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1786.

(2) (a) Zassinovich, G.; Mestroni, G. *Chem. Rev.* **1992**, *92*, 1051. (b) Bianchini, C.; Farnetti, E.; Graziani, M.; Nardin, G.; Vacca, A.; Zanobini, F. *J. Am. Chem. Soc.* **1990**, *112*, 9190. (c) De Martin, S.; Zassinovich, G.; Mestroni, G. *Inorg. Chim. Acta* **1990**, *174*, 9. (d) James, B. B.; Morris, H. R. *J. Chem. Soc., Chem. Commun.* **1978**, 929.

(3) (a) *Comprehensive Organic Synthesis*; Trost, B. W., Ed.; Pergamon Press: Oxford, 1991; Vol. 8, pp 551−553 and references cited therein. (b) Saburi, M.; Ohnuki, M.; Ogasawara, M.; Takahashi, T.; Uchida, Y. *Tetrahedron Lett.* **1992**, *33*, 5783. (c) Sasson, Y.; Blum, J. *J. Org. Chem.* **1975**, *40*, 1887. (d) Sasson, Y. Cohen, M.; Blum, J. *Synthesis* **1973**, 359. (e) Sasson, Y.; Blum, J. *Tetrahedron Lett.* **1971**, 2167.

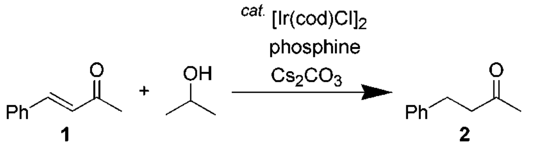
(4) Bhaduri, S.; Sharma, K.; Mukesh, D. *J. Org. Soc., Dalton Trans.* **1992**, *1*, 77.

(5) (a) Beaupere, D.; Bauer, P.; Nadjo, L.; Uzan, R. *J. Organomet. Chem.* **1982**, *238*, C12. (b) Beaupere, D.; Nadjo, L.; Uzan, R.; Bauer, P. *J. Mol. Catal.* **1983**, *18*, 73.

(6) Higashino, T.; Sakaguchi, S.; Ishii, Y. *Org. Lett.* **2000**, *2*, 4193.

10.1021/jo0156722 CCC: $20.00

influenced by the phosphine ligand used. When PPh_3 was added in place of PCy_3, **1** was reduced to give 4-phenyl-2-butanol (60%) as a major product along with **2** (37%) (Table 1, entry 2). It is noteworthy that the use of bidentate phosphine ligands such as 1,3-bis(diphenylphosphino)ethane (dppe) and 1,3-bis(diphenylphosphino)propane (dppp) led to the selective formation of **2**. In particular, **2** was obtained with complete selectivity when the reaction was carried out by the use of dppp as the ligand (Table 1, entry 4). Thus, the selective transfer hydrogenation of α,*β*-unsaturated ketone **1** to saturated one **2** was successfully achieved by the use of an iridium catalyst. Although almost no reaction took place when $[Ir(cod)Cl]_2$ complex was used alone, the reduction proceeded to some extent by the use of $[Ir(cod)Cl]_2$ combined with dppp or Cs_2CO_3 (Table 1, entries 6−8). The use of Na_2CO_3 or Et_3N as base resulted in low yield of **2** (Table 1, entries 9 and 10).

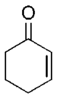
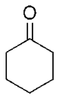
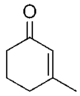
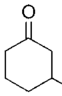
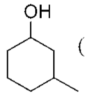
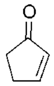
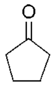
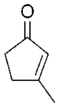
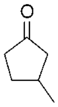
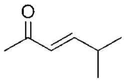
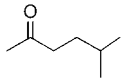
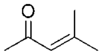
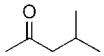
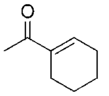
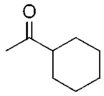
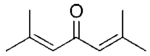
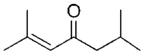
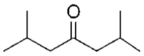
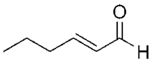
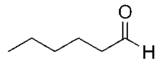
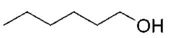


(1)

Table 2 summarizes the results for the transfer hydrogenation of various α,*β*-unsaturated carbonyl compounds using the $[Ir(cod)Cl]_2/dppp/Cs_2CO_3$ system. A variety of α,*β*-unsaturated ketones were reduced to the corresponding ketones in excellent yields except for 3-methyl-2-cyclohexen-1-one, which was reduced to the corresponding alcohol with both carbon−carbon and carbon−oxygen double bonds reduced (Table 2, entries 1−8). 2-Hexenal under these reaction conditions afforded hexanal in 70% selectivity and hexanol (7%) at 75% conversion (Table 2, entry 9).

The present $[Ir(cod)Cl]_2/dppp/Cs_2CO_3$ system was also found to promote the transfer hydrogenation of carbonyl compounds and simple alkenes (Table 3). For instance, the reaction of cyclohexanone (**5**) with 2-propanol catalyzed by the $[Ir(cod)Cl]_2/dppp/Cs_2CO_3$ afforded cyclohexanol (**6**) in good yield (Table 3, entry 1). Acyclic ketones such as 2-octanone, however, were difficult to reduce under these reaction conditions, probably because the resulting 2-octanol is a better hydrogen source than 2-propanol (Table 3, entry 2). Hence, when excess 2-propanol was employed, 2-octanol was obtained in higher yield (Table 3, entry 3). Additionally, styrene was also hydrogenated to ethylbenzene in excellent yield (Table 3, entry 6). Quite recently, an efficient transfer hydrogenation of simple alkynes and alkenes with methanol catalyzed by an hydrido(methoxo)iridium(III) complex has been reported.[7]

Table 2. Transfer Hydrogenation of Various α,*β*-Unsaturated Carbonyl Compounds Catalyzed by $[Ir(cod)Cl]_2$[a]

entry	substrate	conv. (%)	product (selectivity/%)
1		99	 (98)
2[b]		91	 (70)  (25)
3[b]	 3	96	 4 (94)
4[c,d]		79	 (96)
5		99	 (95)
6[d]		90	 (98)
7[c,d]		78	 (96)
8[c,e]		68	 (74)  (26)
9		75	 (70)  (7)

[a] Substrate (0.5 mmol) was allowed to react with 2-propanol (5.0 mmol) in the presence of a catalytic amount of $[Ir(cod)Cl]_2$ (2 mol %), dppp (2 mol %), and Cs_2CO_3 (2 mol %) in toluene (0.5 mL) at 80 °C for 4 h. [b] $[Ir(cod)Cl]_2$ (1 mol %), dppp (1 mol %), Cs_2CO_3 (1 mol %). [c] Cs_2CO_3 (1 mol %). [d] 15 h. [e] 75 °C, 6 h.

Discussion

The selective reduction of conjugated double bonds of α,*β*-unsaturated carbonyl compounds with 2-propanol as a hydrogen source was successfully achieved by the catalysis of $[Ir(cod)Cl]_2$ in combination with dppp and Cs_2CO_3. The most important feature in this reaction is that the resulting ketones were not further reduced to alcohols except in the case of 3-methyl-2-cyclohexenone, although the present catalyst system also promotes the transfer hydrogenation of saturated ketones to alcohols. Thus, we next examined the reduction of a 1:1 mixture of a α,*β*-unsaturated ketone and a saturated one catalyzed by $[Ir(cod)Cl]_2/dppp/Cs_2CO_3$ system. The reaction of a 1:1 mixture of cyclopentenone (**3**) (0.5 mmol) and cyclohexanone (**5**) (0.5 mmol) with 2-propanol (5 mmol) using $[Ir(cod)Cl]_2$ (0.01 mmol) in the presence of dppp (0.01 mmol) and Cs_2CO_3 (0.01 mmol) was performed. Figure 1 shows the time dependence curves for the production of cyclopentanone (**4**) and cyclohexanol (**6**). As expected, the reduction of **3** took place faster compared with that of **5**, suggesting that the iridium complex coordinates preferentially to the double bond of the α,*β*-unsaturated ketone to that of the carbonyl group.

Tani et al. reported that simple alkynes and alkenes were reduced with methanol under the influence of an iridium hydrido(methoxo) complex prepared by the reaction of $[Ir(dpdp)Cl]_2$ (dpdp = 2,2′-bis(diphenylphosphino)-1,1′-biphenyl) with methanol.[7,8] They suggested that an iridium dihydride complex was formed and acted as the real catalyst. The coordination of the iridium complex to

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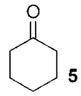
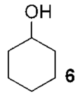
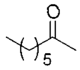
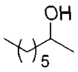
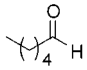
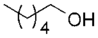
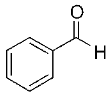
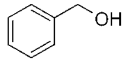
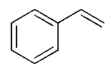
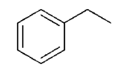
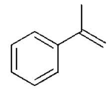
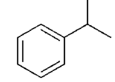
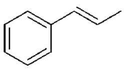
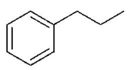
(7) Tani, K.; Iseki, A.; Yamagata, T. *Chem. Commun.* **1999**, 1821.

(8) Tani, K.; Iseki, A.; Yamagata, T. *Angew. Chem. Ind. Ed.* **1998**, *37*, 3381.

Table 3. Transfer Hydrogenation of Several Carbonyl Compounds and Alkenes by the $[Ir(cod)Cl]_2/dppp/Cs_2CO_3$[a]

entry	substrate	conv. (%)	product	(selectivity/%)
1[b]		82		(98)
2[c,d]		38		(97)
3[e,d]		60		(98)
4[f]		97		(94)
5		89		(96)
6[c]		99		(96)
7[d]		68		(92)
8[d]		64		(84)

[a] Reaction was run as shown in Table 2; see footnote *a*. [b] $[Ir(cod)Cl]_2$ (1 mol %), dppp (1 mol %), Cs_2CO_3 (1 mol %). [c] $[Ir(cod)Cl]_2$ (4 mol %), dppp (4 mol %), Cs_2CO_3 (4 mol %). [d] 15 h. [e] 2-Propanol (10 mmol) was used. [f] Cs_2CO_3 (1 mol %).

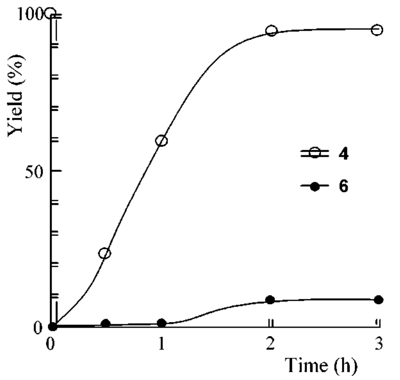
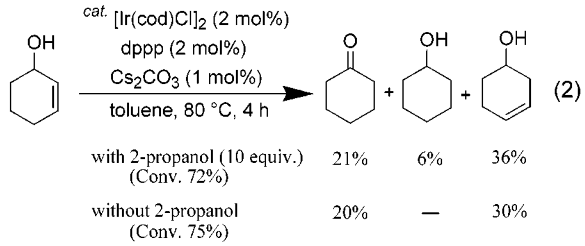


Figure 1. Time-dependence curves for the reduction of a 1:1 mixture of cyclopentenone (**3**) and cyclohexanone (**5**) by the $[Ir(cod)Cl]_2/dppp/Cs_2CO_3$ system. A mixture of **3** (0.5 mmol) and **5** (0.5 mmol) was allowed to react with 2-propanol (5.0 mmol) in the presence of a catalytic amount of $[Ir(cod)Cl]_2$ (0.01 mmol), dppp (0.01 mmol) and Cs_2CO_3 (0.01 mmol) in toluene (0.5 mL) at 80 °C.

alkene followed by hydride insertion gave the corresponding alkane. The reaction pathway of the present transfer hydrogenation by $[Ir(cod)Cl]_2/dppp/Cs_2CO_3$ is not fully confirmed at this stage, but it seems likely that the reaction proceeds through a similar pathway as reported by Tani et al. The reaction may be initiated by the coordination of an iridium hydride complex, generated in situ from $[Ir(cod)Cl]_2$−dppp complex and 2-propanol under the influence of Cs_2CO_3, to α,β-unsaturated carbonyl compound followed by hydrogen transfer to a conjugated double bond giving a saturated carbonyl compound.

Although another reaction path via the formation of allylic alcohol followed by double bond migration to enol is also possible, the formation of allylic alcohol was not observed at all during the reaction course. In addition, the selective conversion of allylic alcohol to carbonyl compound is found to be difficult under these reaction conditions. Treatment of 2-cyclohexen-1-ol by the $[Ir(cod)Cl]_2/dppp/Cs_2CO_3$ system produced a mixture of cyclohexanone, cyclohexanol, and 3-cyclohexen-1-ol in the presence or absence of 2-propanol, respectively (eq 2). These observations suggested that the present reduction of α,β-unsaturated carbonyl compound did not involve the formation of allylic alcohol as an intermediate.



In conclusion, the chemoselective transfer hydrogenation of α,β-unsaturated carbonyl compounds to saturated compounds has been accomplished by the use of the combined catalyst system of $[Ir(cod)Cl]_2/dppp/Cs_2CO_3$. This method was also effective for the reduction of both simple carbonyl compounds and alkenes. Furthermore, in the reaction of a 1:1 mixture of conjugated enone and saturated ketone with 2-propanol catalyzed by the $[Ir(cod)Cl]_2/dppp/Cs_2CO_3$ system, the reduction of the α,β-unsaturated ketone took place in preference to that of the saturated ketone.

Experimental Section

General Procedures. ^1H and ^{13}C NMR spectra were measured at 270 and 67.5 MHz, respectively, in $CDCl_3$ with TMS as the internal standard. IR spectra were measured as films on NaCl plates. GLC analysis was performed with a flame ionization detector using a 1 mm × 30 m capillary column (OV-1). All starting materials were commercially available and used after distillation or recrystallization.

General Procedure for the Reduction of α,β-Unsaturated Carbonyl Compounds with 2-Propanol. To a toluene solution (0.5 mL) of $[Ir(cod)Cl]_2$ (0.005 mmol), dppp (0.005 mmol), and Cs_2CO_3 (0.005 mmol) were added α,β-unsaturated compounds (0.5 mmol) and isopropyl alcohol (5 mmol) under Ar, and then the reaction mixture was stirred at 80 °C for 4 h. After quenching with wet ether, the products were isolated by column chromatography (230−400 mesh silica gel, hexane). After the reaction, the GC and GC−MS analyses were performed. The yields of products were estimated from the peak areas based on the internal standard technique using GC. The products except for 3-cycohexen-1-ol[9] were commercially available and were identified through comparison of the isolated product with an authentic sample.

2,6-Dimethyl-2-hepten-4-one: ^1H NMR ($CDCl_3$/TMS) δ 5.99 (s, 1H), 2.20 (d, $J = 6.7$ Hz, 2H), 2.08−2.05 (m, 1H), 2.07 (s, 3H), 1.81 (s, 3H), 0.85 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR ($CDCl_3$/TMS) δ 201.1, 141.0, 124.1, 53.3, 27.6, 25.1, 22.6, 20.6.

JO0156722

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