An Unusual Example of Base-Free Catalyzed Reduction of C=O and C=NR Bonds by Transfer Hydrogenation and Some Useful Implications

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Received February 1, 2008

A series of Cp*Ir^{III}(NHC) complexes have been used in the catalytic transfer hydrogenation of ketones and imines in *i*PrOH, showing that the reduction of ketones is complete within minutes at room temperature, with the unprecedented feature that the reaction does not need the addition of a base as cocatalyst. This finding implies that aldehydes (a problematic family of substrates for hydrogen transfer) and base-sensitive ketones can be reduced using these catalysts. Furthermore, the catalysts can be utilized in the tandem reduction of chiral aldehydes and their enzymatic dynamic kinetic resolution (DKR), providing moderate asymmetric inductions.

Introduction

Although metal-catalyzed hydrogen transfer reduction of ketones and imines has been widely studied during the last two decades,[1] there is a continuous demand in developing new active catalysts that can achieve such reactions under mild conditions and simple methodologies. Many recent reports have focused efforts on determining the mechanistic aspects of the reaction,[2,3] but the process is far from being fully understood since each new catalytic species seems to behave through a different reaction pattern. A common feature of these reactions is that they involve metal hydrides (monohydrides or dihydrides), and that a base is generally required in order to promote their formation.[2,4] Only in a few cases where the metal–ligand bifunctional mechanism operates, as when chelating amines are used,[5] base-free conditions can be applied, since one of the coordination sites of the ligand is acting as a basic center. Apart from the obvious environmental benefits arising from the design of base-free hydrogen transfer processes, the addition of base often affects the enantioselectivity of the reduction and makes the reaction not suitable for hydrogenation of base-sensitive ketones and aldehydes.

In recent years, a series of Cp*Ir(NHC) complexes have appeared as effective catalysts for C−H activation processes.[6–8] Yamaguchi, Fujita, and co-workers have widely studied the Oppenauer-type oxidation of primary and secondary alcohols with acetone, employing Cp*Ir(III) catalysts.[9] The introduction of N-heterocyclic carbene ligands greatly improved the catalytic performances of such complexes,[8,10] as a consequence of the increasing of electron density at the metal center and the higher reactivity of the iridium-hydride intermediates. In a very recent report, the same group achieved the "ligand-promoted" oxidant-free oxidation of alcohols using a new Cp*Ir(III) species with a 2-hydroxypyridine ligand.[11] At the same time, in our group, a series of Cp*Ir(NHC) complexes were obtained showing high capabilities for intramolecular[12] and catalytic[7] C−H bond activation processes. We described a series of complexes that showed high efficiencies in the deuteration of organic molecules employing methanol-d_4 as deuterium source.[7] For this latter process, the addition of a base is not required in order to achieve high catalytic performance, and we proposed that the reaction proceeded through an O−D rather than C−D activation pathway of the CD_3OD source, possibly through an Ir^{V}(D)(OMe) intermediate.

On the basis of these results, we decided to see if we could widen the scope of the catalytic activity of some of our previously reported "Cp*Ir(NHC)" complexes, since applications in other C−H activation processes were easily envisaged. Here we report the study of a series of "Cp*Ir(NHC)" complexes in the transfer hydrogenation of ketones and aldehydes. The reactions proceed under base-free conditions at room temperature, a feature that we used for the reduction of base-sensitive ketones and aldehydes. We also present an unprec-

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10.1021/om800095t CCC: $40.75
Publication on Web 03/20/2008

Scheme 1

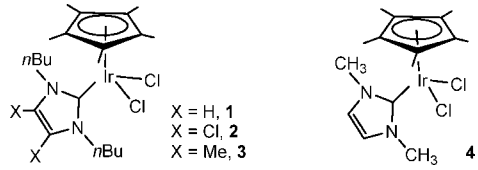


Table 1. Transfer Hydrogenation of Cyclohexanone[a]

entry	catalyst	cat. load. (mol %)	conversion (%)	time	TON
1	**1**	2	>99	15 min	50
2	**1**	0.1	>99	8 h	990
3	**1**	0.01	29	17 h	2900
4	**2**	2	>99	15 min	50
5	**2**	0.1	>99	12 h	990
6	**3**	2	>99	15 min	50
7	**3**	0.1	29	12 h	290
8	**4**	2	>99	15 min	50
9	**4**	0.1	34	5 h	340

[a] Reaction conditions: 0.45 M substrate in *i* PrOH at room temperature. Cat/AgOTf 1:3. Conversions determined by ^{1}H NMR spectroscopy.

edented example of a tandem reduction of a chiral aldehyde and dynamic kinetic resolution of the resulting chiral alcohol.

Results and Discussion

As we previously mentioned, Yamaguchi, Fujita and coworkers recently described an elegant example of a "ligand-promoted" dehydrogenation of alcohols using a Cp*Ir(III) species with a 2-hydroxypyridine ligand.[11] Dehydrogenative oxidations of alcohols can proceed in the absence of a base, because the reaction is the inverse of the hydrogenation of ketones using H_2, a process that also generally occurs in the absence of an added base. To test if such oxidation could be possible in a transfer hydrogenation process, for which a base is generally required, we tried the Oppenauer-type oxidation of 2-butanol to 2-butanone using acetone and Cp*IrCl$_2$(I$^{n\mathrm{Bu}}$), **1** (I$^{n\mathrm{Bu}}$ = 1,3-di*n*-butyl-imidazolylidene) as catalyst (2 mol %). AgOTf was added in order to activate the catalyst. Remarkably, the reaction proceeded to completion in 1 h at room temperature, without addition of base as cocatalyst. This result prompted us to perform a more detailed study of the inverse reaction, namely the reduction of ketones and imines by alcohols, using the catalysts **1**−**4** shown in Scheme 1.

Table 1 shows the results on the transfer hydrogenation of cyclohexanone in *i*PrOH using **1**−**4** as catalysts. All manipulations were carried out in the presence of air. For the activation of the catalysts addition of AgOTf was necessary in order to remove the halide ligands and form the corresponding triflate species. The isolation of the triflate compound **1a** (Scheme 2), and its use under the same catalytic conditions did not show any differences in the activities obtained, compared to those displayed in Table 1. For all the catalysts used, the conversion of cyclohexanone into cyclohexanol is complete after 15 min at room temperature with catalyst loadings of 2 mol %. The reaction proceeded to completion without the addition of any external base. Lowering the catalyst loading to 0.1 mol %, resulted in a significant lowering of the catalytic productivity, although the conversions were quantitative when catalysts **1** and **2** were used after 8 and 12 h, respectively (entries 2 and 5). A catalyst loading of 0.01 mol % results in a high TON of 2900, although a low conversion is achieved (29%, entry 3). Under the same reaction conditions, the complexes [Cp*IrCl$_2$]$_2$ and Cp*IrCl$_2$(PMe$_3$) were completely ineffective, which suggests that the higher electron donating power of the NHC ligands

Scheme 2

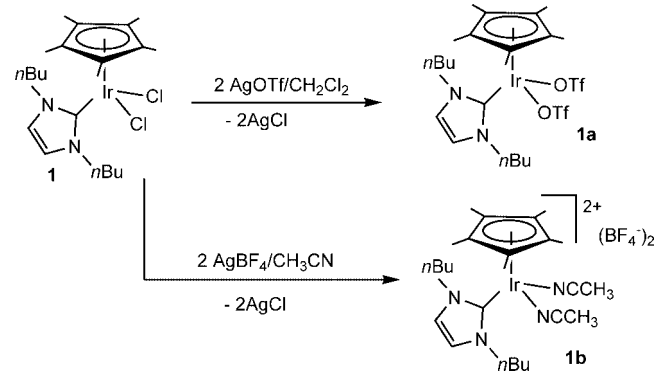


Table 2. Transfer Hydrogenation of Ketones, Aldehydes, and Imines[a]

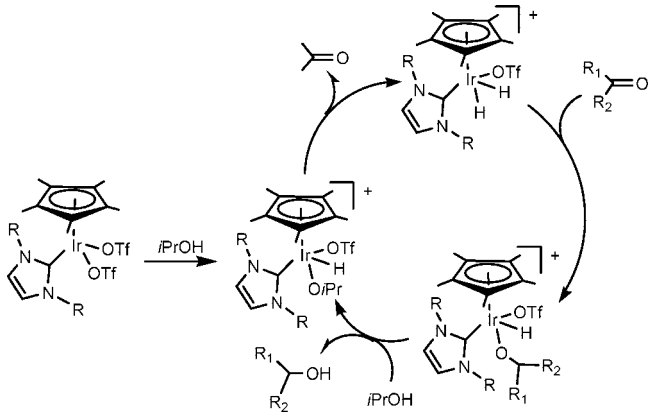
entry	substrate	cat.	load. (mol %)	yield (%)	time	TON
1	2-butanone	**1**	2	>99	2 h	50
2		**1**	0.1	73	22 h	730
3		**2**	0.1	22	12 h	220
4		**3**	0.1	6	12 h	60
5		**4**	2	60	3 h	30
6	benzophenone	**1**	2	94	15 min	47
7		**1**	0.1	50	8 h	500
8		**2**	0.1	10	12 h	100
9		**3**	0.1	9	12 h	90
10		**4**	2	92	5 h	46
11		**4**	0.1	30	5 h	300
12	acetophenone	**1**	2	90	15 min	45
13		**1**	0.1	50	8 h	500
14		**2**	0.1	3	12 h	30
15		**3**	0.1	0	12 h	0
16		**4**	2	76	5 h	38
17		**4**	0.1	3	5 h	30
18	benzylphenylketone	**1**	2	>99	15 min	50
19		**1**	0.1	76	21 h	760
20	2-phenylpropionaldehyde	**1**	2	>99	15 min	50
21		**1**	0.1	87	48 h	870
22	benzaldehyde	**1**	2	>99	30 min	50
23		**1**	0.1	85	48 h	850
24	benzene-1,4-dicarboxaldehyde	**1**	2	>99	30 min	50
25		**1**	0.1	>99	48 h	990
26	*N*-benzylideneaniline	**1**	0.1	>99	48 h	990

[a] Reaction conditions: 0.45 M substrate in *i* PrOH at room temperature. Cat/AgOTf 1:3. Yields determined by ^{1}H NMR spectroscopy.

compared to phosphines plays a decisive role in the reaction. We still do not have a clear explanation to justify the lower activity of catalysts **3** and **4**, because we would expect that their NHC ligands provided a similar or even higher electron donation than I$^{n\mathrm{Bu}}$, but the fact is that I$^{n\mathrm{Bu}}$ has persistently provided the best catalytic activities in other C−H activation processes that we have studied.[7]

To check the scope of the catalytic properties of **1**−**4**, we performed the reduction of a series of aliphatic and aromatic ketones (Table 2, entries 1–17). Compound **1** resulted an efficient catalyst for the reduction of all the ketones tested (2-butanone, benzophenone, and acetophenone), and almost quantitative conversions were achieved in 15 min when a catalyst loading of 2 mol % was used. For lower catalyst loadings, longer reaction times were needed, and the reactions failed to achieve completion. Both the N-bound wingtips and the substituents on the C4 and C5 positions of the azole ring have important effects in the catalytic performances of the complexes. Complexes with unsubstituted NHCs offer the best catalytic results (compounds **1** and **4**), and the presence of the *N*-*n*-butyl groups seems to enhance the catalytic behavior over the compounds with

Scheme 3



N-methyl groups. Catalyst **1** resulted the most active, and the reduction of aliphatic ketones (cyclohexanone and 2-butanone) was more effective than the reduction of the aromatic ones (acetophenone, benzophenone).

To check the applicability of our complexes, we used compound **1** in the reduction of deoxybenzoin (benzylphenylketone), a series of aldehydes, and *N*-benzylideneaniline. The fact that **1** promoted the base-free catalytic reduction of these new substrates is an important issue because deoxybenzoin is a base-sensitive ketone that produces *cis*-stilbene under basic reductive conditions. Besides, the reduction of aldehydes by transfer hydrogenation is a difficult challenge because aldehydes tend to undergo metal-mediated decarbonylation and base-mediated aldol condensation. The imine was chosen because we wanted to widen the scope of the catalyst using a substrate that is normally more inert toward hydrogen-transfer processes.

Again, we did not observe any differences in catalytic activity when compound **1** was used in the presence of AgOTf, or when we used the bistriflate complex **1a** by reaction of **1** with AgOTf (Scheme 2). However, when we prepared the dicationic bis-acetonitrile adduct **1b** and used it as catalyst, we observed that its activity was significantly lower, even negligible for some of the substrates used.

The fact that **1a** is a better catalyst than **1b** may be due to the higher electron density on the neutral metal fragment than on the dicationic one. This would be favoring the oxidative addition of *i*PrOH to generate a 'Cp*Ir^{V}(NHC)H(O*i*Pr)' intermediate, if we assume that an O−H activation of the alcohol has been produced, as we previously proposed for the deuteration of organic molecules using MeOD as deuterium source.[7] Although we do not have direct and conclusive evidence to support a detailed mechanism, we believe that the one depicted in Scheme 3 is the most likely to happen. The oxidative addition of O−H bonds to Ir complexes is a well-known process,[13] and "Cp*Ir^{V}" species have long been proposed from the theoretical[14] and experimental[15] points of view. We believe that the dihydride intermediate may be justifying our observations that, under mild reaction conditions, **1a** promotes the oxidant-free oxidation of terminal alcohols to aldehydes with loss of H_2 (these results are at a preliminary stage and will be published in the near future) in a process that is similar to that recently described by Fujita.[11]

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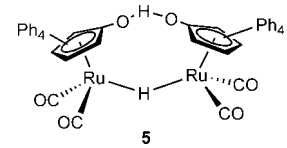
Scheme 4



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We thought that base-free transfer hydrogenation processes may have some other applications in the design of concerted catalytic reactions. For example, the combination of hydrogen transfer reactions with the enzymatic dynamic kinetic resolution to generate chiral acetates is one of the possible good choices because it is known that the use of a base in these reactions usually affects the performance of the enzyme and may cause side reactions, such as epoxide formation.[16] In a remarkable work, Jung and co-workers described the concerted catalytic reactions for the conversion of prochiral ketones to chiral acetates through a tandem process implying transfer hydrogenation (acetone to alcohol) and acetylation through a DKR process (alcohol to chiral acetate).[17] For this concerted process, the hydride-bridged bisruthenium complex **5** (Scheme 4) was used,[18] because it had previously shown high activities in hydrogen transfer reactions and DKR of alcohols.[18,19] In the design of such concerted reactions, an important limitation is that a proper hydrogen donor has to be utilized; the most widely used one, *i*PrOH, is also an effective substrate in lipase acetylation processes, so a sterically hindered alcohol such as 2,6-dimethylheptan-4-ol has to be used.[17]

In a very recent work, it was shown that "Cp*Ir(NHC)" can be used as efficient catalysts for the dynamic kinetic resolution (DKR) of secondary alcohols, and the fact that the reaction can proceed under base-free conditions constituted one of the main goals of the work.[20] With this precedent, we thought that compound **1a** could be a good candidate for the tandem reduction of C═O functionalities to alcohols followed by the enzymatic DKR process. One of the main drawbacks in the design of this concerted reaction is that the use of 2,6-dimethylheptan-4-ol (available in an 80% purity) as hydrogen donor requires its previous purification through enzymatic acetylation of the impurities and further fractional distillation,[17] thus complicating the reaction workup. Aiming the search for a simple and efficient concerted process, we thought that the use of aldehydes instead of ketones could overcome the problem of using *i*PrOH as hydrogen donor, since presumably primary alcohols should be more easily acetylated than *i*PrOH because they are less sterically hindered. Very recently, Backvall and co-workers described the enzymatic DKR of chiral primary alcohols using a Ru catalyst.[21] It was proposed, that the

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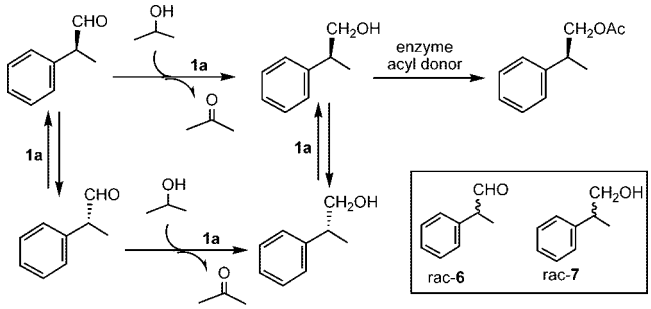
Scheme 5



racemization proceeded through a (i) metal-catalyzed dehydrogenation of the alcohol, (ii) enolization of the aldehyde formed, and (iii) metal-catalyzed readdition of hydrogen to the aldehyde. We thought that our Ir catalyst could also be active in the metal mediated steps implied in this reaction.

With all this in mind, we designed a reaction implying the reduction of a chiral aldehyde to the corresponding primary alcohol, followed by the chiral resolution of the racemic mixture by the enzymatic DKR process (Scheme 5). As a model substrate, and for comparative purposes, we used a racemic mixture of the β-branched chiral aldehyde **6**, which by reduction in the presence of *i*PrOH generates alcohol **7** (Table 2, entries 20 and 21), one of the alcohols used by Backvall's group.[21]

For a rapid screening of the reaction conditions leading to the best results, we decided to use combinations of two lipases (*Candida antarctica* lipase B, CALB, and Amano lipase PS-D I from *Burkholderia cepacia*) and two acyl donors (*p*-chlorophenyl acetate and *p*-chlorophenyl 3-[4-(trifluoromethyl)phenyl]propanoate)). The use of the widely utilized alkenyl acetates was discarded because the formation of aldehydes or ketones after the acyl transfer process can interfere with the hydrogen transfer catalyst.

Table 3 shows the results that we obtained for the screening of the conditions for the concerted process, using **1a** as catalyst. Entries 1 and 2 show that the lipase CALB is completely ineffective in the kinetic resolution of the racemic mixtures of **6** and **7**, although the conversions to the acylated compounds were quantitative. In the case of the concerted reaction starting from **6** (entry 1), this result is particularly interesting because it indicates that the acylation of **6** is selective over the acylation of *i*PrOH, which is not taking place under these reaction conditions, thus validating this hydrogen donor for future studies on the concerted reduction/kinetic resolution of chiral aldehydes. The Amano lipase PS-D I has been used for the kinetic resolution of various primary alcohols.[21,22]Although we expected that the more sterically hindered trifluoromethylpropanoate would afford good ee values, we observed that the reaction starting from **6** did not show any asymmetric induction (entry 5). In the absence of the metal catalyst, the kinetic resolution process of the racemic mixture of alcohol **7** provided a moderate ee value of 69%. This result contrasts with the high ee values obtained by Backvall's group for the same alcohol under similar reaction conditions. For the reaction combining the lipase PS-D I and chlorophenylacetate at 80 °C, we obtained the best result with a conversion of 82% and a moderate ee of 61% (entry 3). Lowering of the temperature to 70 °C afforded a negligible ee of 5% (entry 4).

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Conclusions

The results described here show that Cp*Ir(NHC) complexes are excellent catalysts for the reduction of ketones, aldehydes, and imines under very mild conditions. More remarkably, the catalytic activity of the complexes does not need to be accompanied by the addition of an external base as cocatalyst, which represents the first example of a base-free transfer hydrogenation process not using a metal-hydride procatalyst. In a recent work, we described the catalytic H/D exchange of organic molecules achieved by Cp*Ir(NHC) catalysts.[7] The process implied facile intermolecular C−H activation under mild reaction conditions, and alcohols and ketones were among the most active organic substrates for this type of catalytic exchange. Also, experimental approaches[15] and theoretical calculations on the dehydrogenation of alkanes by "Cp*IrH(PH_3)" complexes suggest that the alkane (RH) oxidatively adds to the metal providing a "$CpIr^{V}H_2(R)(PH_3)$" complex which reductively eliminates H_2.[23] In our case, the oxidative addition is even more favorable because the NHC ligands are more basic than phosphines. In this sense, we can consider that the oxidative addition of *i*PrOH may provide the active intermediate in the catalytic cycle.

This base-free transfer hydrogenation process has interesting implications because it can be applied to the reduction of base-sensitive ketones (deoxybenzoin) and aldehydes. Furthermore, the reaction can be combined with enzymatic DKR processes, because the absence of the base avoids the formation of undesired byproduct in the transesterification process. In our work, we have shown an unprecedented example of a concerted reaction implying the transfer hydrogenation of a chiral aldehyde and the enzymatic DKR of the resulting alcohol. The reaction is even more interesting if we consider that the most widely used hydrogen donor (*i*PrOH) can be used without any interference with the acetylation process. Although our preliminary studies provided moderate values of ee, studies in order to improve these results are underway.

Experimental Section

General Procedures. $[Cp^*IrCl_2]_2$,[24] 1,3-di*n*-butyl-4,5-dimethylimidazolium chloride,[25] and compounds **1**, **2**, and **4**[7] were prepared according to literature procedures. All other reagents were used as received from commercial suppliers. NMR spectra were recorded on Varian Innova 300 and 500 MHz, using $CDCl_3$ and acetone-d_6 as solvents. Electrospray Mass Spectra (ESI-MS) were recorded on a QTOF I (quadrupole-hexapole TOF) mass spectrometer with an orthogonal Z-spray-electrospray interface, in the case of compound **1b**, and on a Micromass Quatro LC instrument, for compound **3**. In all cases, nitrogen was employed as drying and nebulizing gas. Elemental analyses were carried out on a Euro-EA3000 Eurovector Analyzer.

Synthesis of 1a. Compound **1** (100 mg, 0.17 mmol) and AgOTf (90 mg, 0.35 mmol) were introduced into a Schlenk flask and dried under vacuum for 10 min. Freshly distilled CH_2Cl_2 (5 mL) was added to the solid mixture and the suspension was stirred at room temperature for 2 h. The resulting reaction mixture was filtered using a cannula and the solvent was removed under vacuum. Compound **1a** was obtained as a yellow-brown oil. Yield: 130 mg (94%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (s, 2H, C*H* imidazole),

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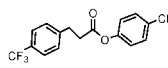
Table 3. Conversions of 6 and 7 to Chiral Acetates

Entry	Substrate	Acyl donor	Lipase	T (°C)	Time (h)	Conv. (%)	ee (%)
1	*Rac*-**6**		CALB	70	24	>99	0
2	*Rac*-**7**			70	16	>99	0
3	*Rac*-**6**		PS-D I	80	24	82	61
4	*Rac*-**6**			70	24	60	5
5	*Rac*-**6**			80	36[a]	70	0
6	*Rac*-**7**[b]			80	36[a]	50	69

[a] Lipase added in two batches, 15 mg lipase first and an additional amount of 5 mg after 24 h. [b] In the absence of catalyst. Reaction conditions for CALB: 0.25 mmol substrate, 0.75 mmol acyl donor, 0.375 mmol 2-propanol, 2 mol % catalyst (**1a**), 7.5 mg of lipase in 0.8 mL of toluene. For PS-D I: 0.5 mmol substrate, 0.6 mmol acyl donor, 0.75 mmol 2-propanol, 2 mol % catalyst (**1a**), 20 mg of lipase in 5 mL of toluene. Conversions determined by ^{1}H NMR. Enantiomeric excesses determined by ^{1}H NMR after preparation of the corresponding Mösher's esters.

4.04 (td, $^3J_{H,H}$ = 12.5 Hz, $^2J_{H,H}$ = 4.5 Hz, 2H, CH_2 *n*Bu), 3.91 (td, $^3J_{H,H}$ = 12.5 Hz, $^2J_{H,H}$ = 4.5 Hz, 2H, CH_2 *n*Bu), 1.99 (m, 2H, CH_2 *n*Bu), 1.77 (m, 2H, CH_2 *n*Bu), 1.64 (s, 15H, CH_3 Cp*), 1.47 (sp, $^3J_{H,H}$ = 7.5 Hz, 4H, CH_2 *n*Bu), 1.01 (t, $^3J_{H,H}$ = 7.5 Hz, 6H, CH_3 *n*Bu). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.16 (*C*-Ir), 122.57 (*C*H imidazole), 121.19 (q, J = 318.1 Hz, *C*F_3), 88.86 (*C*$_5$(CH$_3$)$_5$), 49.85 (*n*-Bu), 32.44 (*n*-Bu), 20.32 (*n*-Bu), 13.91 (*n*-Bu), 9.63 (C$_5$(*C*H$_3$)$_5$).

Synthesis of 1b. $AgBF_4$ (84 mg, 0.42 mmol) was added to a solution of compound **1** (81 mg, 0.14 mmol) in CH_3CN. The mixture was stirred at room temperature for 30 min and then filtered through a pad of Celite. After concentration to ca. 2 mL, diethylether was added and the resulting yellow solid was filtered off. Yield: 110 mg (>99%). ^{1}H NMR (300 MHz, acetone-d_6): δ 7.76 (s, 2H, C*H* imidazole), 4.20 (m, 4H, CH_2 *n*Bu), 2.83 (s, 6H, CH_3CN), 2.02 (m, 4H, CH_2 *n*Bu), 1.91 (s, 15H, CH_3 Cp*), 1.57 (q, $^3J_{H,H}$ = 7.8 Hz, 4H, CH_2 *n*Bu), 1.04 (t, $^3J_{H,H}$ = 7.4 Hz, 6H, CH_3 *n*Bu). ^{13}C NMR (75 MHz, acetone-d_6): δ 146.56 (*C*-Ir), 123.75 (*C*H imidazole), 117.04 (CH$_3$*C*N), 94.77 (*C*$_5$(CH$_3$)$_5$), 50.71 (*n*-Bu), 33.37 (*n*-Bu), 19.98 (*n*-Bu), 13.40 (*n*-Bu), 8.47 (C$_5$(*C*H$_3$)$_5$), 3.52 (*C*H$_3$CN). TOF MS. ES+, 10V. (*m*/*z*, fragment): 295.1447, $[M]^{2+}$.

Synthesis of 3. Silver oxide (29 mg, 0.125 mmol) was added to a solution of 1,3-di-*n*-butyl-4,5-dimethylimidazolium chloride (61 mg, 0.25 mmol) in CH_2Cl_2. The solution was stirred at room temperature for 1 h and then $[Cp^*IrCl_2]_2$ (100 mg, 0.125 mmol) was added. The mixture was heated at 50 °C for 4 h and then filtered through a pad of Celite. The solvent was evaporated and the crude solid purified by column chromatography. The pure compound **3** was eluted with dichloromethane/acetone 9:1 and precipitated in a mixture of diethylether/*n*-pentane to give an orange solid. Yield: 35 mg (23%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.50 (m, 2H, -CH_2 *n*-Bu), 3.61 (m, 2H, -CH_2 *n*-Bu), 2.16 (s, 6H, C−CH_3 imidazole), 2.09 (m, 2H, *n*-Bu), 1.52 (m, 4H, *n*-Bu), 1.49 (s, 15H, CH_3 Cp*), 1.29 (m, 2H, *n*-Bu), 0.90 (t, 6H, *n*-Bu). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.04 (*C*-Ir), 126.09 (*C*-CH$_3$ imidazole), 88.36 (*C*$_5$(CH$_3$)$_5$), 49.38 (*n*-Bu), 33.96 (*n*-Bu), 20.30 (*n*-Bu), 13.98 (*n*-Bu), 9.67 (C-*C*H$_3$ imidazole), 9.04 (C$_5$(*C*H$_3$)$_5$). Anal. Calcd. for $C_{23}H_{39}Cl_2IrN_2$: C, 45.53; H, 6.48; N, 4.62. Found: C, 45.60; H, 6.48; N, 4.61. ESI-MS Cone 15V. (*m*/*z*, fragment): 571.2, $[M]^+$.

General Procedure for Transfer Hydrogenation Catalysis. A solution of the substrate in *i*PrOH (0.45M) was prepared, and the corresponding catalyst (2, 0.01, or 0.1 mol %) and AgOTf (catalyst/AgOTf, 1:3) were subsequently added. The resulting mixture was stirred at room temperature. Aliquots were extracted from the reaction vessels and added to a NMR tube containing 0.5 mL of $CDCl_3$. Conversions were determined by ^{1}H NMR spectroscopy.

General Procedure for Conversion of Aldehydes to Chiral Acetates. Determination of the Enantiomeric Excess. When CALB was used as lipase, a 100 mL Schlenk flask was charged under nitrogen with 0.25 mmol of the corresponding substrate, 0.75 mmol acyl donor, 0.375 mmol 2-propanol, 2 mol % catalyst **1a**, 7.5 mg of CALB, and toluene (0.8 mL). The mixture was stirred at 70 °C.

When Amano Lipase PS-D I was used as lipase, a 100 mL Schlenk was charged under nitrogen with 0.5 mmol of the corresponding substrate, 0.6 mmol acyl donor, 0.75 mmol 2-propanol, 2 mol % catalyst **1a**, 20 mg of Amano Lipase PS-D I, and toluene (5 mL). The mixture was stirred at 80 °C.

In all cases, conversions were determined by ^{1}H NMR spectroscopy. All volatile compounds were removed under reduced pressure. Silica gel chromatography (hexanes/ethyl acetate = 95:5) afforded the chiral acetate as a colorless oil. Hydrolysis with a 1 M methanolic solution of NaOH gave the corresponding alcohol, which was purified by column chromatography (hexanes/ethyl acetate = 9:1). Once isolated, a solution of the alcohol in degassed CH_2Cl_2 was introduced into a Schlenk. *N*,*N*′-Dicyclohexylcarbodiimide (1.5 equiv.), R-(+)-α-Methoxy-α-trifluoromethylphenylacetic acid (1.2 equiv.) and a catalytic amount of 4-dimethylaminopyridine were added under nitrogen. The solution was stirred at room temperature until complete consumption of the alcohol. The mixture was then filtered through a pad of Celite and the volatile compounds were removed under reduced pressure. Silica gel chromatography (hexanes/ethyl acetate = 95:5) afforded a mixture of the diastereomeric esters. Enantiomeric excesses (ee) were determined by ^{1}H NMR analysis of the diastereomeric ratio. The determination of the ee values by HPLC or GC using similar conditions as previously reported by other groups[21] did not provide satisfactory results because the enantiomers could not be resolved.

Acknowledgment. We gratefully acknowledge financial support from the MEC of Spain (Projects CTQ2005-05187) and Bancaixa (P1.1B2007-04). R.C. thanks the Spanish Ministerio de Educación y Ciencia for a fellowship.

OM800095T