J|A|C|S
ARTICLES
Published on Web 03/12/2003

Isolation and Crystal Structure of a Water-Soluble Iridium Hydride: A Robust and Highly Active Catalyst for Acid-Catalyzed Transfer Hydrogenations of Carbonyl Compounds in Acidic Media

Tsutomu Abura,[†,‡] Seiji Ogo,*[,†] Yoshihito Watanabe,[§] and Shunichi Fukuzumi*[,†]

Contribution from the Department of Material and Life Science, Graduate School of Engineering, Osaka University, PRESTO & CREST, Science and Technology Corporation (JST), Suita 565-0871, Japan, Department of Structural Molecular Science, The Graduate University for Advanced Studies, Myodaiji, Okazaki 444-8585, Japan, and Department of Chemistry, Graduate School of Science, Nagoya University, Chikusa-ku, Nagoya 464-8602, Japan

Received October 5, 2002; E-mail: ogo@ap.chem.eng.osaka-u.ac.jp

Abstract: This paper reports the isolation and structural determination of a water-soluble hydride complex $[Cp^*Ir^{III}(bpy)H]^+$ (**1**, $Cp^* = \eta^5$-C_5Me_5, bpy = 2,2′-bipyridine) that serves as a robust and highly active catalyst for acid-catalyzed transfer hydrogenations of carbonyl compounds at pH 2.0−3.0 at 70 °C. The catalyst **1** was synthesized from the reaction of a precatalyst $[Cp^*Ir^{III}(bpy)(OH_2)]^{2+}$ (**2**) with hydrogen donors HCOOX (X = H or Na) in H_2O under controlled conditions (2.0 < pH < 6.0, 25 °C) which avoid protonation of the hydrido ligand of **1** below pH ca. 1.0 and deprotonation of the aqua ligand of **2** above pH ca. 6.0 (pK_a value of **2** = 6.6). X-ray analysis shows that complex **1** adopts a distorted octahedral geometry with the Ir atom coordinated by one η^5-Cp*, one bidentate bpy, and one terminal hydrido ligand that occupies a bond position. The isolation of **1** allowed us to investigate the robust ability of **1** in acidic media and reducing ability of **1** in the reaction with carbonyl compounds under both stoichiometric and catalytic conditions. The rate of the acid-catalyzed transfer hydrogenation is drastically dependent on pH of the solution, reaction temperature, and concentration of HCOOH. The effect of pH on the rate of the transfer hydrogenation is rationalized by the pH-dependent formation of **1** and activation process of the carbonyl compounds by protons. High turnover frequencies of the acid-catalyzed transfer hydrogenations at pH 2.0−3.0 are ascribed not only to nucleophilicity of **1** toward the carbonyl groups activated by protons but also to a protonic character of the hydrido ligand of **1** that inhibits the protonation of the hydrido ligand.

Introduction

The chemistry in aqueous media is presently undergoing very rapid growth because of many potential advantages such as industrial applications (e.g., introduction of new biphasic processes) and reaction-specific pH selectivity.[1,2] In this area, development of reagents to be used under acidic (or basic) conditions is a worthy endeavor owing to applications in synthesis in the presence of functional groups that are sensitive to basic (or acidic) conditions.

For the reduction of carbonyl compounds under acidic conditions in aqueous media, sodium cyanoborohydride ($NaBH_3CN$) is frequently utilized as a noncatalytic reducing agent.[3] However, serious precautions in handling are required since $NaBH_3CN$ is flammable and a very hygroscopic solid and highly toxic HCN is formed as a byproduct of the reduction. Hydrogenation and transfer hydrogenation are useful methods for catalytic reductions of carbonyl compounds in organic solvents,[4] though instability of metal−hydride species in acidic media has precluded definitive characterization of active catalysts in aqueous media.

We preliminarily reported pH-dependent transfer hydrogenations of a variety of carbonyl compounds catalyzed by an in-situ-formed hydride species $[Cp^*Ir^{III}(bpy)H]^+$ (**1**, $Cp^* = \eta^5$-

[†] Osaka University, PRESTO & CREST, JST.
[‡] The Graduate University for Advanced Studies.
[§] Nagoya University.

(1) Reviews: (a) Joó, F. In *Catalysis by Metal Complexes*; James, B. R., Leeuwen, P. W. N. M., Series Eds.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 2001; Vol. 23, Aqueous Organometallic Catalysis, p 300. (b) Cornils, B.; Herrmann, W. A. In *Aqueous-Phase Organometallic Catalysis*; Wiley-VCH: Weinheim, Germany, 1998; p 615. (c) Li, C.-J.; Chan, T.-H. In *Organic Reactions in Aqueous Media*; John Wiley & Sons: New York, 1997; p 199. (d) Koelle, U. *Coord. Chem. Rev.* **1994**, *135*/*136*, 623−650. (e) Herrmann, W. A.; Kohlpaintner, C. W. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1524−1544.

(2) (a) Ogo, S.; Nakai, H.; Watanabe, Y. *J. Am. Chem. Soc.* **2002**, *124*, 597−601. (b) Ogo, S.; Abura, T.; Watanabe, Y. *Organometallics* **2002**, *21*, 2964−2969 and references therein; (c) Nakai, H.; Ogo, S.; Watanabe, Y. *Organometallics* **2002**, *21*, 1674−1678. (d) Makihara, N.; Ogo, S.; Watanabe, Y. *Organometallics* **2001**, *20*, 497−500. (e) Ogo, S.; Makihara, N.; Watanabe, Y. *Organometallics* **1999**, *18*, 5470−5474. (f) Ogo, S.; Chen, H.; Olmstead, M. M.; Fish, R. H. *Organometallics* **1996**, *15*, 2009−2013. (g) Lo, H. C.; Leiva, C.; Buriez, O.; Kerr, J. B.; Olmstead, M. M.; Fish, R. H. *Inorg. Chem.* **2001**, *40*, 6705−6716. (h) Joó, F.; Kovács, J.; Bényei, A. C.; Kathó, Á. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 969−970.

(3) (a) Borch, R. F.; Bernstein, M. D.; Durst, H. D. *J. Am. Chem. Soc.* **1971**, *93*, 2897−2904. (b) Lane, C. F. In *Selections from the Aldrichimica Acta*; Aldrich Chemical Co., Inc.: Milwaukee, WI, 1984; pp 67−74. (c) Lane, C. F. *Synthesis* **1975**, 135−146. (d) Carruthers, W. In *Some Modern Methods of Organic Synthesis*; Cambridge University Press: New York, 1987; pp 475−476.

C_5Me_5, bpy = 2,2′-bipyridine).[5] However, the definitive structure of **1** has yet to be disclosed. Besides, low turnover frequencies (TOFs = (mol of product formed/mol of catalyst)/1 h) of the transfer hydrogenations in acidic media should have been improved.

Herein, we report isolation of **1**, whose structure was unequivocally determined by X-ray analysis. Complex **1** acts as a robust and highly active catalyst for the transfer hydrogenations of carbonyl compounds under optimized conditions. The robust ability of **1** in acidic media is discussed on the basis of pH-dependent properties of the hydrido ligand and stability of **1** under acidic conditions. The reducing ability of **1** is investigated under stoichiometric and catalytic conditions that are optimized for the pH of the solution, reaction temperature, and concentration of HCOOH as a hydrogen donor. The isolation and structural determination of **1** provide excellent opportunity to elucidate the mechanism of high TOFs of the pH-dependent transfer hydrogenations catalyzed by **1**.

Experimental Section

Materials and Methods. All experiments were carried out under an Ar atmosphere by using standard Schlenk techniques and a globebox. The manipulations in the acidic media were carried out with plastic- and glasswares (without metals). D_2O (99.9% D) was purchased from Cambridge Isotope Laboratories, and 65% DNO_3/D_2O (99% D) and DCOONa (99% D) were purchased from Isotec Inc.; these reagents were used as received. All carbonyl compounds used in this study (highest purity available) were purchased from Aldrich Chemicals Co. Purification of water (18.2 MΩ cm) was performed with a Milli-Q system (Millipore; Milli-RO 5 plus and -Q plus). The ^{1}H NMR spectra were recorded on Varian VRX-300S and JEOL JNM-AL300 spectrometers at 20 °C. H_2 and CO_2 gases were determined by a Shimadzu GC-8A (He carrier, Unibeads column, 60/80 2 m, GL Sciences Inc.) equipped with a thermal conductivity detector. A Nissin magnetic stirrer (model SW-R700) was used.

pH Adjustment. In a pH range of 1.0−10.0, the pH value of the solutions was determined by a pH meter (TOA, HM-18E) equipped with a pH combination electrode (TOA, GS-5015C). The pH of the solution was adjusted by using 0.01−3.00 M HNO_3/H_2O and 0.01−3.00 M $NaOH/H_2O$ without buffer. During the reaction, a stainless steel-micro pH probe (IQ Scientific Instruments, Inc., PH15-SS) was dipped in the reaction mixture at 70 °C under Ar atmosphere, and the pH of the solution was monitored by a pH meter (IQ Scientific Instruments, Inc., IQ200). It was confirmed that the pH of the solution does not change during the course of the reactions under the conditions of this study. To determine the exact pH values, the ^{1}H NMR experiments were performed by dissolving the samples in HNO_3/H_2O in an NMR tube (diameter = 5.0 mm) with a sealed capillary tube (diameter = 1.5 mm) containing 3-(trimethylsilyl)propionic-2,2,3,3-d_4 acid sodium salt (TSP, 500 mM, as the reference with the methyl proton resonance set at 0.00 ppm) dissolved in D_2O (for deuterium lock). Values of pD were corrected by adding 0.4 to the observed values.[6] In the case of biphasic media, the pH value of the aqueous phase is adopted.

[Cp*Ir^{III}(bpy)H](PF$_6$) [1(PF$_6$)]. A reaction of [Cp*Ir^{III}(bpy)(OH_2)](SO_4) [**2**(SO_4), 60 mg, 0.1 mmol] and HCOONa (2720 mg, 40 mmol) in H_2O (20 mL) at pH 5.0 at 70 °C for 15 min provides a yellow solution of water-soluble mononuclear hydride complex $[\mathbf{1}]^+$. To the solution was added $NaPF_6$ (17 mg, 0.1 mmol) in H_2O (20 mL), and the mixture was stirred for 1 min giving an orange powder of **1**(PF_6), which was collected by filtration, washed with water, and dried in vacuo. The powder was recrystallized from methanol/diethyl ether to provide air-sensitive orange crystals of **1**(PF_6). Yield: 35% based on **2**(SO_4). ^{1}H NMR (300 MHz, in D_2O, reference to TPS, 25 °C): δ −11.80 (s, 1H), 1.78 (s, 15H), 7.62 (t, 2H), 8.11 (t, 2H), 8.29 (d, 2H), 8.90 (d, 2H).

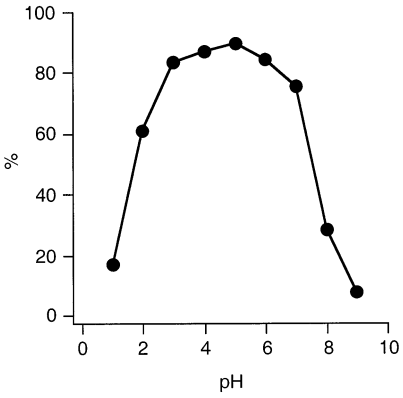


Figure 1. pH-dependent formation ratio of $[\mathbf{1}]^+$ prepared from the reaction of **2**(SO_4) (5 μmol) with 100 equiv (500 μmol) of HCOOH in D_2O (1 mL) at 25 °C for 5 min.

Transfer Hydrogenations. Water-soluble and water-insoluble carbonyl compounds (0.32 mmol), **2**(SO_4) (1.0 mg, 1.6 μmol), and HCOOH (6.7 M HCOOH 0.25 mL, 1.6 mmol) were dissolved in H_2O (3 mL) at pH 1.0−10.0 under Ar atmosphere. The mixture was vigorously stirred (1000 rpm, Nissin magnetic stirrer model SW-R700) at 25−90 °C. After 1−4 h, it was cooled to 0 °C, and the resulting mixture was analyzed by ^{1}H NMR. Water-soluble products (entries **a**, **d**, and **e**) were isolated by salting-out with NaCl and extraction with Et_2O. Water-insoluble products (entries **b**, **c**, and **g**) were isolated by extraction with Et_2O. Furthermore, the water-insoluble products (entries **c** and **g**) were also isolated by using Whatman phase separators 1PS (silicone-treated filter paper) without organic solvents. It was confirmed that the transfer hydrogenations do not occur in the absence of **2** or HCOOH (as blank experiments).

X-ray Crystallographic Analysis. Crystallographic data for **1**(PF_6) have been deposited with the Cambridge Crystallographic Data Center as supplementary publication No. CCDC-193541. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB21EZ, U.K. [fax, (+44)1223-336-033; e-mail, deposit@ccdc.cam.ac.uk]. Measurements were made on a Rigaku/MSC Mercury CCD diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.7107). All calculations were performed using the teXsan crystallographic software package of the Molecular Structure Corp. Crystal data, data collection parameters, structure solution and refinement, atomic coordinates, anisotropic displacement parameters, bond lengths, and bond angles are given in the Supporting Information.

Results and Discussion

Isolation and Characterization of 1. In a pH 2.0−6.0 region at 25°C, a mononuclear hydride complex $[\mathbf{1}]^+$ was synthesized from the reaction of [Cp*Ir^{III}(bpy)(OH_2)](SO_4) [**2**(SO_4)] with HCOOX (X = H or Na) through β-hydrogen elimination with the evolution of CO_2 that was confirmed by GC analysis (see Experimental Section). Complex $[\mathbf{1}]^+$ has high solubility in water (20 mg/mL at pH 5.0 at 25 °C). In this study, HCOOH was used not only as a hydrogen donor but also as an acid to prepare the acidic pH of the solution. Figure 1 shows the pH-

(4) (a) Noyori, R.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 40−73. (b) Ohkuma, T.; Ishii, D.; Takeno, H.; Noyori, R. *J. Am. Chem. Soc.* **2000**, *122*, 6510−6511. (c) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97−102. (d) Casey, C. P.; Singer, S. W.; Powell, D. R.; Hayashi, R. K.; Kavana, M. *J. Am. Chem. Soc.* **2001**, *123*, 1090−1100. (e) Casey, C. P.; Singer, S. W.; Powell, D. R. *Can. J. Chem.* **2001**, *79*, 1002−1011. (f) Süss-Fink, G.; Faure, M.; Ward, T. R. *Angew. Chem., Int. Ed.* **2002**, *41*, 99−101.
(5) Ogo, S.; Makihara, N.; Kaneko Y.; Watanabe, Y. *Organometallics* **2001**, *20*, 4903−4910.
(6) (a) Glasoe, P. K.; Long, F. A. *J. Phys. Chem.* **1960**, *64*, 188−190. (b) Mikkelsen, K.; Nielsen, S. O. *J. Phys. Chem.* **1960**, *64*, 632−637.

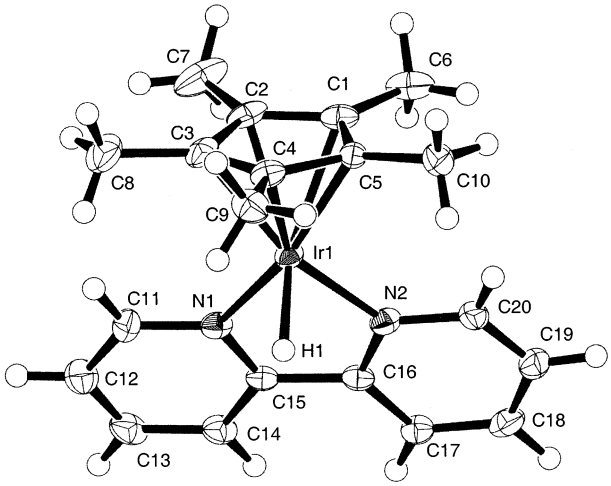


Figure 2. ORTEP drawing (50% probability) of **1**(PF_6). The anion (PF_6) is omitted for clarity.

dependent formation of **1** from the reaction of **2** with 100 equiv of HCOOH (in the absence of reducible ketones) at 25°C for 5 min.

The influence of pH on the formation of **1** is explained by pH-dependent structural changes of **1**, **2**, and HCOOH as follows: (i) Below pH ca. 1.0, the protonation of the hydrido ligand of **1** leads to the formation of **2** with the evolution of H_2 that was confirmed by GC analysis (eq 1, **M** = Cp*Ir^{III}bpy). (ii) Above pH 3.6, HCOOH acts as $HCOO^-$ to bind the iridium center since the pK_a value of HCOOH at the studied concentration is 3.6 (eq 2). (iii) Above pH 6.6 (= pK_a value of **2**), complex **2** is predominantly deprotonated to form a hydroxo complex $[Cp^*Ir^{III}(bpy)(OH)]^+$ that hardly reacts with HCOOH (eq 3).

$$\underset{\mathbf{1}}{[\mathbf{M}-\mathrm{H}]^+} + \mathrm{H}^+ \xrightarrow[\mathrm{H_2O}]{\mathrm{pH} < \text{ca. } 1.0} \underset{\mathbf{2}}{[\mathbf{M}-\mathrm{OH_2}]^{2+}} + \mathrm{H_2} \qquad (1)$$

$$\mathrm{HCOOH} \rightleftharpoons \mathrm{HCOO^-} + \mathrm{H^+} \qquad (2)$$

$$\underset{\mathbf{2}}{[\mathbf{M}-\mathrm{OH_2}]^{2+}} \rightleftharpoons [\mathbf{M}-\mathrm{OH}]^+ + \mathrm{H}^+ \qquad (3)$$

It was confirmed by ^{1}H NMR that complex **1** is quite stable below 70 °C under an Ar atmosphere at pH 2.0−6.0 in the absence of reducible carbonyl compounds. Above 90 °C, however, complex **1** is slowly decomposed to unidentified compounds accompanied by Ir−C(Cp*) bond cleavage. It is noteworthy that the thermostability of M−C(Cp*) bonds of $[Cp^*M(bpy)(H_2O)]^{2+}$ (M = Co^{III}, Rh^{III}, and Ir^{III}) in acidic media (pH 2.0−6.0) is in order Ir−C(Cp*) > Rh−C(Cp*) ≫ Co−C(Cp*). It is expected that the Ir−N bonds are stabilized by a chelate effect of the bpy ligand compared with those of a monodentate pyridine ligand.

Crystal Structure of 1(PF_6). Orange crystals of **1**(PF_6) used in X-ray analysis (Figure 2) were obtained by diffusion of diethyl ether into a methanol solution of **1**(PF_6) at ambient temperature (see Experimental Section).

To our knowledge, this is the first crystal structure of a mononuclear highly active catalyst for the transfer hydrogenations of carbonyl compounds under acidic conditions in aqueous media.[7] Crystal data, data collection parameters, and structure refinement for **1** are listed in Table 1. Selected bond lengths and angles for **1** are listed in Table 2.

Table 1. Summary of Crystal Data, Data Collection Parameters, and Structure Refinement for **1**(PF_6)

empirical formula	$C_{20}H_{24}F_6IrN_2P$
fw	629.61
cryst color	orange
cryst dimens (mm)	0.20 × 0.25 × 0.24
cryst system	monoclinic
a (Å)	8.924(1)
b (Å)	15.025(2)
c (Å)	15.823(2)
β (deg)	96.569(6)
V (Å^3)	2107.7(4)
space group (No.)	$P2_1/c$ (14)
Z	4
D_{calc} (g cm^{-3})	1.984
F_{000}	1216
μ(Mo Kα) (cm^{-1})	64.89 K
radiation (λ, Å)	Mo Kα (0.7107)
temp (°C)	−150
$2\theta_{max}$ (deg)	54.9
abs corr method	numerical
no. of reflcns obsd (all, 2θ < 54.9°)	4674
no. of params	274
R^a	0.049
R_w [b]	0.062
R1[c]	0.030
goodness of fit indicator, S^d	0.98
max shift/error in final cycle	0.002
max peaks in final diff map (e Å^{-3})	1.45
min peaks in final diff map (e Å^{-3})	−0.72

[a] $R = \sum(F_o^2 - F_c^2)/\sum F_o^2$. [b] $R_w = [\{\sum\omega(Fo^2 - Fc^2)^2/\sum\omega(F_o^2)^2\}]^{1/2}$. [c] R1 = $\sum||F_o| - |F_c||/\sum|F_o|$ [for >2.0σ(I) data]. [d] Goodness of fit indicator, $S = [\sum w(|F_o| - |F_c|)^2/(N_o - N_v)]^{1/2}$ (N_o = number of observations; N_v = number of variables).

Table 2. Selected Bond Lengths (//Å) and Angles (ϕ/deg) for **1**(PF_6)

Ir1−H1	1.73(5)	Ir1−N1	2.069(4)	Ir1−N2	2.069(4)
Ir1−C1	2.235(5)	Ir1−C2	2.254(5)	Ir1−C3	2.179(5)
Ir1−C4	2.171(5)	Ir1−C5	2.160(5)	C1−C2	1.495(7)
C1−C5	1.453(7)	C2−C3	1.445(7)	C3−C4	1.430(7)
C4−C5	1.437(7)	N1−Ir1−N2	77.0(2)	H1−Ir1−N1	84(1)
H1−Ir1−N2	84(1)	C1−Ir1−C2	36.9(2)	C1−Ir1−C5	38.6(2)
C2−Ir1−C3	38.0(2)	C3−Ir1−C4	38.4(2)	C4−Ir1−C5	38.7(2)

Complex **1** adopts a distorted octahedral coordination which is surrounded by one η^5-Cp* ligand, one bidentate bpy ligand, and one terminal hydrido ligand (H1) that occupies a bond position. The atomic coordinates (x, y, z) of H1 were refined in the X-ray analysis. The Ir1−H1 bond length of **1** is 1.73(5) Å, which is close to Ir−H bond lengths (average 1.77 Å) of dinuclear μ-hydride complex $[(Cp^*Ir^{III})_2(\mu\text{-}H)_3]^+$ previously determined by X-ray analysis.[2a] The distances between Ir atom and carbons of the Cp* ring of complex **1** in the solid state are not equivalent; the distances of Ir1−C1 and Ir1−C2 [2.235(5) and 2.254(5) Å, respectively] trans to the hydrido ligand are longer than those of Ir1−C3, Ir1−C4, and Ir1−C5 [2.179(5), 2.171(5), and 2.160(5) Å, respectively] trans to the bpy ligand. This result indicates that the hydrido ligand has a greater trans influence than the bpy ligand. The torsion angle between the least-squares plane of Cp* and that of bpy is 66.3(3)°.

(7) (a) Slugovc, C.; Mereiter, K.; Trofimenko, S.; Carmona, E. *Angew. Chem., Int. Ed.* **2000**, *39*, 2158−2160. (b) Klei, S. R.; Tilley, T. D.; Bergman, R. G. *J. Am. Chem. Soc.* **2000**, *122*, 1816−1817. (c) Gruet, K.; Crabtree, R. H.; Lee, D.-H.; Liable-Sands, L.; Rheingold, A. L. *Organometallics* **2000**, *19*, 2228−2232. (d) Dorta, R.; Togni, A. *Organometallics* **1998**, *17*, 3423−3428.

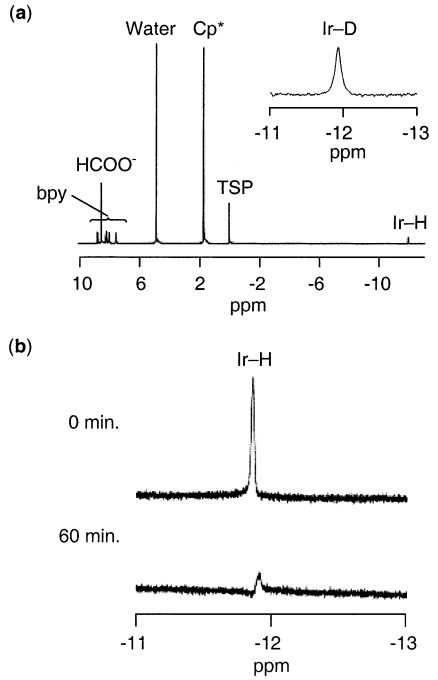


Figure 3. (a) ^{1}H NMR spectrum of $[\mathbf{1}]^+$ in D_2O at 25 °C at pD 5.0. TSP: the reference with the methyl proton resonance set at 0.00 ppm. The inset shows the ^{2}H NMR spectrum of the D-labeled $[\mathbf{1}]^+$ in D_2O (reference to D_2O at 4.78 ppm). (b) H/D exchange of **1** (5 μmol) with D^+ (0.1 M DNO_3/D_2O, 1 mL, at pD 5.0) at 25 °C monitored by ^{1}H NMR for 60 min. The signal at −11.80 ppm corresponds to the hydrido ligand of **1**.

pH-Dependent Properties of the Hydrido Ligand of 1. Figure 3a shows ^{1}H NMR spectrum of $[\mathbf{1}]^+$ in D_2O at pD 5.0 (pD = pH meter reading + 0.4)[6] at 25 °C.

The signal at −11.80 ppm corresponds to the hydrido ligand of **1**. To establish the origin of the hydrido ligands of **1**, the synthesis of D-labeled **1** {$[Cp^*Ir^{III}(bpy)D]^+$} by a reaction of **2** with DCOONa in H_2O at pH 5.0 for 15 min at 25 °C has been carried out (**M** = $Cp^*Ir^{III}bpy$):

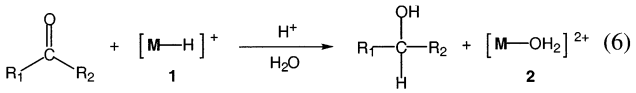
$$\underset{\mathbf{2}}{[\mathbf{M}{-}OH_2]^{2+}} + DCOO^- \xrightarrow[H_2O]{\text{pH 5.0}} \underset{\text{D-labeled } \mathbf{1}}{[\mathbf{M}{-}D]^+} + CO_2 + H_2O \quad (4)$$

The ^{2}H NMR spectrum shows that the deuterium atom is incorporated in **1** (Figure 3a). Complex **1** undergoes an H/D exchange with D^+ in a pD range of 2.4−6.4 (eq 5).[8] Figure 3b shows the result of H/D exchange in 60 min at pD 5.0 at 70 °C.

In the pD range of 2.4−6.4, the lower the pD of the solution, the faster is the rate of the H/D exchange; i.e., the rate of the H/D exchange is dependent on D^+ concentration. These results suggest that the hydrido ligand of **1** exhibits a protonic character.

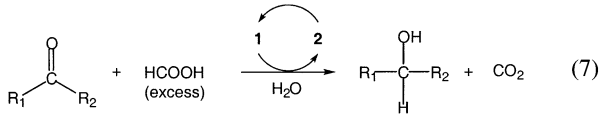
$$\underset{\mathbf{1}}{[\mathbf{M}{-}H]^+} \overset{\text{pD 2.4−6.4}}{\rightleftharpoons} \underset{\text{D-labeled } \mathbf{1}}{[\mathbf{M}{-}D]^+} \quad (5)$$

Reducing Ability of 1 in Acidic Media. We have investigated the reducing ability of **1** toward cyclohexanone (**a**) as an example of water-soluble ketones and acetophenone (**b**) as an example of water-insoluble ketones in water and in biphasic media (**b** + water), respectively. Under stoichiometric conditions (**1**/ketones = 1/1) in the absence of HCOOH, **a** and **b** are reduced to cyclohexanonol (yield: 43%) and 1-phenylethanol (yield: 40%) in 20 min at pH 2.0 at 70 °C as shown in eq 6 (where **M** = $Cp^*Ir^{III}bpy$).



(6)

On the other hand, under catalytic conditions (eq 7, **1**/ketones/HCOOH = 1/200/1000), complex **1** catalyzes the transfer hydrogenations of **a** and **b** to yield the corresponding alcohols (yield: 99%) in 2 h at pH 2.0 at 70 °C.



(7)

^{1}H NMR experiments revealed that the labeled hydrogen atoms (D) are incorporated into the ketones when DCOONa is used as the hydrogen donor in the transfer hydrogenations.

Optimized Conditions of Transfer Hydrogenations. The TOFs of the acid-catalyzed transfer hydrogenation are drastically dependent on the pH of the solution, reaction temperature, and concentration of HCOOH. Because of operational simplicity, optimization of the conditions of the transfer hydrogenation is carried out with the air-stable precatalyst **2** and HCOOH. Figure 4 shows pH-dependent profiles of TOFs of the transfer hydrogenations of cyclohexanone (**a**, closed circle) and acetophenone (**b**, open circle).[9]

The rate of transfer hydrogenations of carbonyl compounds examined in this study shows a sharp maximum around pH 2.0. The pH dependence should be explained not only by the stability of **1** in the acidic media but also by the activation process of the carbonyl compounds by protons as follows: (i) Compound **b** is not reduced by **1** under stoichiometric conditions (**1**/**b**/

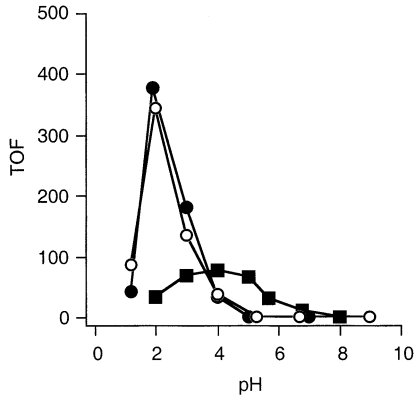
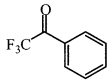
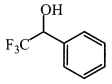
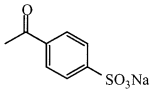
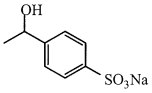


Figure 4. (●) pH-dependent profile of TOFs for the transfer hydrogenation of **a** (0.32 mmol) with **2**(SO_4) (1.6 μmol) and 1000 equiv (1.6 mmol) of HCOOH in water (3 mL) at 70 °C for 15 min. (○) pH-dependent profile of TOFs for the transfer hydrogenation of **b** (0.32 mmol) with **2**(SO_4) (1.6 μmol) and 1000 equiv (1.6 mmol) of HCOOH in water (3 mL) at 70 °C for 15 min. (■) pH-dependent profile of TOFs for the transfer hydrogenation of **b** (0.32 mmol) with [(η^6-C_6Me_6)Ru^{II}(bpy)(H_2O)] (SO_4) (1.6 μmol) and 1000 equiv (1.6 mmol) of HCOOH in water (3 mL) at 70 °C for 15 min.

(8) (a) Balzarek, C.; Weakley, T. J. R.; Kuo, L. Y., Tyler D. R. *Organometallics* **2000**, *19*, 2927−2931. (b) Balzarek, C.; Tyler, D. R. *Angew. Chem., Int. Ed.* **1999**, *38*, 2406−2408. (c) Trost, B. M. *Chem.—Eur. J.* **1998**, *4*, 2405−2412.

(9) Conditions: **2**/carbonyl compounds/HCOOH = 1/200/1000, pH 2.0, 70 °C.

Table 3. Transfer Hydrogenation of Water-Soluble Carbonyl Compounds (**a**, **d**, **e**, and **f**) and Water-Insoluble Carbonyl Compounds (**b**, **c**, and **g**) with $[Cp^*Ir^{III}(bpy)(H_2O)]^{2+}$ as a Catalyst Precursor and HCOOH as a Hydrogen Donor in Water and in Biphasic Media at pH 2.0[a]

	substrate	product	TOF[b,c]	*t* (h)	yield (%)
(a)			376	1	99[c] (90[d])
(b)			343	1	97[c] (97[e])
(c)			525	1	99[c] (89,[e] 40[f])
(d)			150	4	99[c] (51[d])
(e)			481	1	98[c] (35[d])
(f)			419	1	99[c] (-[g])
(g)			203	3	98[c] (96,[e] 43[f])

[a] The reaction was carried out at **70** °C using a ketone (0.32 mmol) in H_2O (3 mL) with **2**/ketones/HCOOH = 1/200/1000. [b] Turnover frequency: (mol of product/mol of **2**)/h. [c] Determined by ^1H NMR. [d] Isolated yield after salting-out with NaCl and extraction with Et_2O. [e] Isolated yield after extraction with Et_2O. [f] Isolated yield by using Whatman phase separators 1PS (silicone-treated filter paper) without organic solvents. [g] Not isolated by extraction with Et_2O.

HCOOH = 1/1/0) in methanol at 60 °C, though an addition of 1% (v/v) of trifluoroacetic acid (TFA) as a proton source to the methanol solution initiates a reduction of **b** to 1-phenylethanol in 10% yield.[10] (ii) The TOF (525) of transfer hydrogenation of an acetophenone derivative containing an electron-withdrawing group (2,2,2-trifluoroacetophenone, **c**) is higher than the TOF (343) of transfer hydrogenation of acetophenone (**b**) at pH 2.0 at 70 °C (Table 3).

In addition, as shown in Figure 4, the TOF (343) of the transfer hydrogenations of **b** catalyzed by **2** and HCOOH at pH 2.0 (open circle)[9] is significantly higher than the TOF (75) of previously reported transfer hydrogenation of **b** catalyzed by a ruthenium complex $[(\eta^6\text{-}C_6Me_6)Ru^{II}(bpy)(H_2O)](SO_4)$ and HCOONa at pH 4.0 (open triangle).[2b,11]

Figure 5 reveals temperature-dependent TOFs in the transfer hydrogenations of **a** (closed circle) and **b** (open circle). The TOFs of the transfer hydrogenations are drastically increased above 70 °C. The catalytic reactions were carried out at 70 °C because complex **1** is slowly decomposed above 90 °C under even Ar atmosphere (vide supra).

Furthermore, Figure 6 shows TOFs depending upon concentrations of HCOOH used in the transfer hydrogenations of **a**

(10) The addition of TFA mainly induces the protonation of the hydrido ligand of **1** to generate H_2.
(11) Conditions: Ru catalyst/**b**/HCOONa = 1/200/6000, pH 4.0, 70 °C.

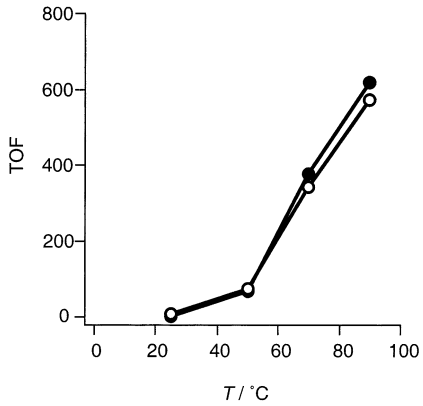


Figure 5. (●) Temperature-dependent TOFs of the transfer hydrogenation of **a**. (○) Temperature-dependent TOFs of the transfer hydrogenation of **b**.

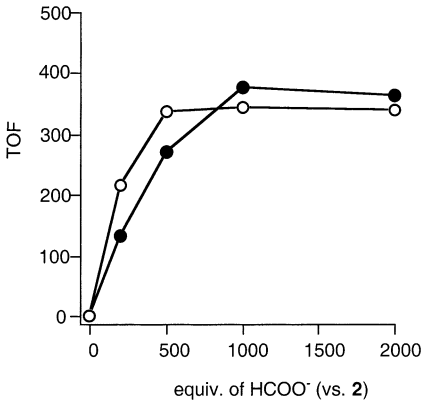


Figure 6. (●) TOFs depending upon the number of moles of $HCOO^-$ of the transfer hydrogenation of **a**. (○) TOFs depending upon the number of moles of $HCOO^-$ of the transfer hydrogenation of **b**.

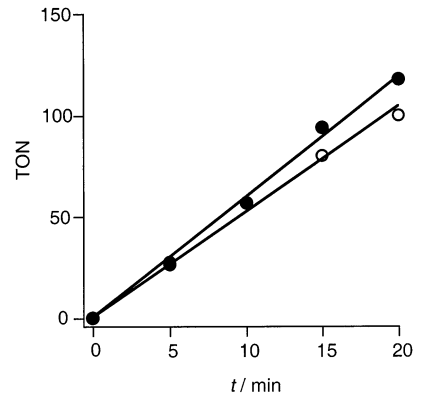


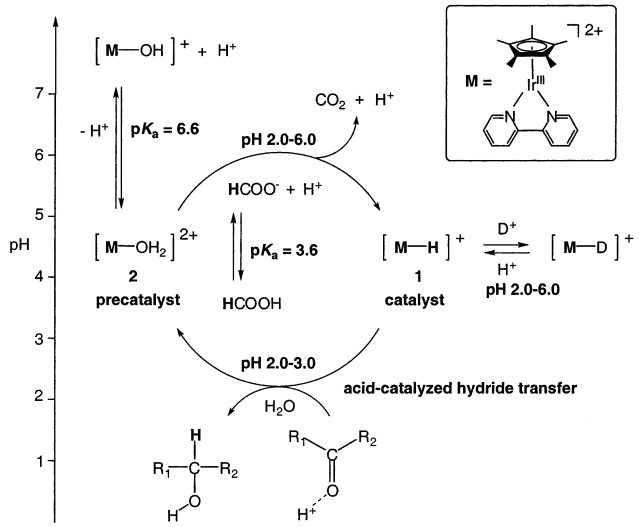
Figure 7. (●) Time course of the TONs of the transfer hydrogenation of **a**. (○) Time course of the TONs of the transfer hydrogenation of **b**.

(closed circle) and **b** (open circle) at pH 2.0 at 70 °C. The TOFs of the transfer hydrogenations of carbonyl compounds examined in this study saturate at a 1/200/1000 ratio of **2**/ketones/HCOOH.

Figure 7 shows the time course of the turnover numbers (= TONs, mol of product formed/mol of catalyst) in the transfer hydrogenations of **a** (closed circle) and **b** (open circle) under the optimized conditions (pH 2.0, 70 °C, 1/200/1000 ratio of **2**/carbonyl compounds/HCOOH).

Table 3 demonstrates the transfer hydrogenations of a variety of water-soluble and water-insoluble carbonyl compounds under the optimized conditions. The water-soluble cyclic ketone (cyclohexanone, **a**) is converted to the corresponding alcohol much more efficiently than a water-soluble straight chain ketone

Scheme 1



(2-butanone, **d**). The transfer hydrogenation of a water-soluble keto acid (pyruvic acid, **e**) also occurs easily. In our previous paper,[9] we reported that compounds **d** and **e** cannot be reduced by in-situ-generated **1** under unoptimized conditions (pH 5.0, 25 °C, **1**/**d** or **e**/HCOOH = 1/10/50). The rate of transfer hydrogenation of an acetophenone derivative with a water-soluble ligand (4-acetylbenzenesulfonic acid sodium salt, **f**) in water is faster than that of acetophenone (**b**) in biphasic media. A water-insoluble bulky cyclic ketone (α-tetralone, **g**) is also reduced. In addition, under the conditions of this study, the water-soluble and water-insoluble aldehydes can be reduced similarly, but the water-soluble and water-insoluble esters cannot be reduced.

Mechanism of High TOFs. As shown in Figure 4, the TOFs of the acid-catalyzed transfer hydrogenation are drastically dependent on the pH of the solution. Scheme 1 summarizes the effect of pH on the formation of **1** (at pH 2.0−6.0) and also on the acid-catalyzed hydride transfer (at pH 2.0−3.0). The remarkable stability of **1** is attributed to the protonic character of the hydrido ligand that prevents the protonation of the hydrido ligand. In conclusion, the high TOFs of the acid-catalyzed transfer hydrogenations should result not only from the nucleophilicity of **1** toward the carbonyl groups activated by protons but rather from the robust ability of **1** under the present acidic conditions.

Acknowledgment. Financial support of this research by the Ministry of Education, Science, Sports, and Culture, Japan Society for the Promotion of Science, Grant-in-Aid for Scientific Research to S.O. (13640568) and S.F. (11228205), is gratefully acknowledged. We thank Professor K. Isobe (Osaka City University) and emeritus Professor A. Nakamura (Osaka University) for valuable discussions.

Supporting Information Available: Crystallographic information. This material is available free of charge via the Internet at http://pubs.acs.org.

JA0288237