Cyclopentadienone Iridium Bipyridyl Complexes: Acid-stable Transfer Hydrogenation Catalysts

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Abstract

The synthesis, structure, and reactivity of a series of cyclopentadienone and hydroxycyclopentadienyl 4,4'-dimethylbipyridine (dmbpy) iridium complexes ($C_5Tol_2Ph_2O$)(dmbpy)IrCl **1**, [($C_5Tol_2Ph_2OH$)(dmbpy)IrCl][OTf] **2** ($C_5Tol_2Ph_2O$)(dmbpy)IrH **3**, and [($C_5Tol_2Ph_2OH$)(dmbpy)IrH][OTf] **4** are described. The Ir(I) complexes **1** and **3** are active catalyst precursors for transfer hydrogenation of aldehydes, ketones, and N-heterocycles with HCO_2H/Et_3N under mild conditions. Model studies implicate the cationic iridium hydride, [($C_5Tol_2Ph_2OH$)(dmbpy)IrH][OTf] **4** as a key intermediate, as **4** reacts readily with acetone to generate isopropanol. Selectivity over hydrogenation of alkenes is enhanced compared to other Shvo-type catalysts, and only modest C=C hydrogenation observed when adjacent to polarizing functional groups. Catalytic hydrogenation likely proceeds by a metal-ligand bifunctional mechanism similar to related cyclopentadienone complexes.

Introduction

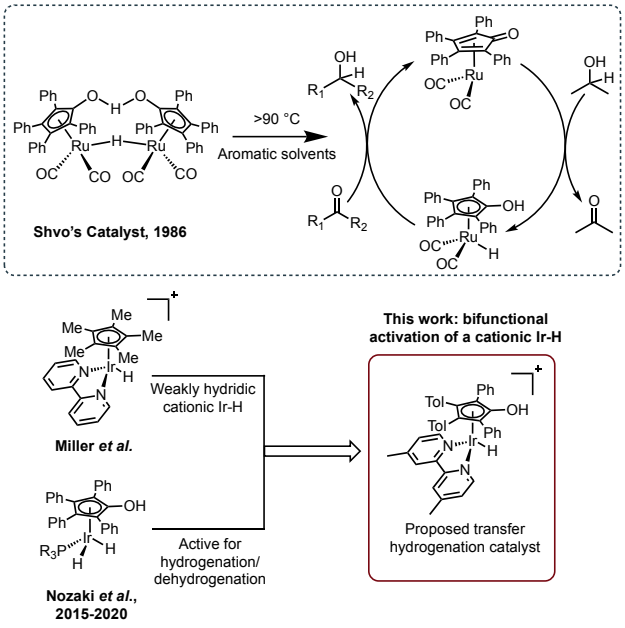


Figure 1. Known cyclopentadienone-metal complexes relevant to the current work

Bifunctional molecular catalysts, employing ligands that cooperatively activate substrates, have enabled new patterns of reactivity.[1,2] Since the first report in 1986[3], a rich body of work has evolved describing the use of "Shvo's dimer" [$Ru_2(CO)_4(C_4Ph_4COHOCC_4Ph_4(\mu\text{-}H)$] (Figure 1) as a precatalyst in the hydrogenation of a wide range of unsaturated substrates.[4] These complexes can effect the hydrogenation of polarized substrates by both molecular hydrogen and by transfer hydrogenations from isopropanol and formic acid. The mechanism of hydrogen transfer from the hydrogenated catalyst has been studied at length,[4,5] and implicate the key role of the hydroxycyclopentadienyl ligand in the bifunctional activation and hydrogenation of polar substrates. Several analogues bearing modified cyclopentadienone ligands have emerged, including complexes of iron,[6,7] rhenium[8], and molybdenum[9] as well as a more distantly-related manganese phenol complex.[10]

Nozaki *et al.* reported a class of cyclopentadienone-iridium complexes bearing phosphine ligands that catalyze hydrogenation and dehydrogenation reactions between 150-200 °C.[11–14] Related Cp*(bpy)IrH^+ complexes are efficient catalysts for transfer hydrogenation in water at low pH.[15–17] In organic solvents, Cp*(bpy)IrH^+ is unreactive toward aldehydes,[15] which was attributed to the modest hydride donating ability ($\Delta G_{H\text{-}(MeCN)}$ ≥60 kcal/mol) of these cationic Ir hydrides.[18,19] However, in the presence of visible light, Cp*(bpy)IrH^+ complexes are effective in hydride transfer reactions as the hydride donating ability is enhanced by photoexcitation[18,20]. We sought to test the hypothesis that modestly hydridic cationic Ir hydrides bearing hydroxycyclopentadienyl ligands might be more generally reactive towards polar substrates in non-aqueous conditions due to bifunctional activation.

Results and Discussion

The synthesis of the Ir cyclopentadienone complexes was carried out by a modification of the procedure described by Nozaki et al.[12] Addition of 4,4'-dimethylbipyridine (dmbpy) to the air-stable but insoluble $[(C_5Tol_2Ph_2O)IrCl]_n$ occurs heterogeneously in methanol to generate the orange solid $(C_5Tol_2Ph_2O)(dmbpy)IrCl$ (**1**), which is indefinitely stable in air, either as a dry solid or in solution. The ^1H NMR spectra of **1** in aprotic solvents is poorly resolved with line broadening in the aromatic region (Figure S2). Mass spectrometry and elemental analysis confirm the bulk identity and purity of **1**.

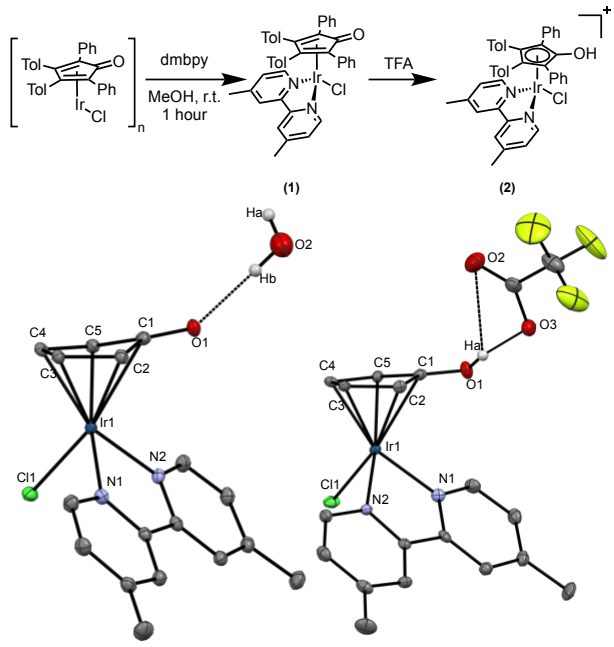


Figure 2. Synthesis and crystal structure of **Ir^I-Cl, 1 (left) and Ir^{III}-Cl, 2 (right)** hydrogens and phenyl rings on the cyclopentadienone are omitted for clarity.

Crystals of **1** were grown in the presence of 1-5 % methanol or water in acetonitrile. The solid-state structure of **1** (Figure 2, left) is consistent with NMR and mass spectra. The presence of a coordinating water in the crystal structure suggests that adventitious H-bonding to the cyclopentadienone motif may be responsible for the changes in ^1H NMR spectral quality upon addition of protic co-solvents.

Treatment of **1** with trifluoroacetic acid (TFA) produces an immediate color change from orange to bright yellow and yields the cationic $[(C_5Tol_2Ph_2OH)(dmpby)IrCl]^+$ (**2**) resulting from protonation of the cyclopentadienone ligand of (**1**). The structure of complex **2**, obtained from x-ray diffraction of crystals grown from acetonitrile solution, shows lengthening of the C1-O1 bond and contraction of the C1-Ir bond relative to **1** (Table 1). The hydroxycyclopentadienyl ring of **2** is more planar than the cyclopentadienone of **1**, consistent with aromatization of the ring and formal intramolecular 2-electron transfer to form an η-5 hydroxycyclopentadienyl bound to an Ir^{III} center. The structural features of the cyclopentadienone/hydroxycyclopentadienyl ligands of **1** and **2** are comparable to those reported by Nozaki *et al.*[21] for the analogous phosphine ligated structures.

Table 1. Selected lengths and angles from SC-XRD structures of Ir^I-Cl and Ir^{III}-Cl

	(1)	(2)
C1-O1 bond length (Å)	1.236	1.286
C1-Ir bond length (Å)	2.404	2.300
∠C2-C1-C5 (°)	103.7	106.9

Attempts to hydrogenate **1** with H_2 or isopropanol at modest temperatures and pressures (below 80 °C, 1 atm H_2) failed to generate an Ir-H complex. Instead, treatment of **1** with sodium formate in methanol generated the dark red Ir^I-H $(C_5Tol_2Ph_2O)(dmbpy)IrH$ **3** as evidenced by a ^1H NMR resonance at $\delta = -12.07$ ppm in benzene that is attributable to the Ir^I-H hydride. The ^1H NMR spectrum of **3** is broad in aprotic solvents, but the spectral quality improves by the addition of methanol. Subtle downfield shifts in the methyl and hydride signals are observed upon the addition of 1-10 % methanol.

Treatment of the Ir^I-H **3** with 10 equivalents of [DMFH][OTf] yields an immediate conversion of the dark red Ir^I-H to a pale yellow solution of $[(C_5Tol_2Ph_2OH)(dmpby)IrH]^+$ **4**. The ^1H NMR spectra of **4** exhibit a hydride resonance at -10.87 ppm (C_6D_6, Figure S6). This Ir^{III}-H resonance persists in the presence of excess [DMFH][OTf] even after 24 h in C_6D_6, indicating that the Ir^{III}-H of **4** is remarkably stable to strong acid (Figure 3, details in the SI). This is consistent with the Cp* congeners that require photoexcitation to display any reactivity with strong acids in acetonitrile, indicating a modestly hydridic metal hydride.[18]

The cationic Ir^{III}-H **4** reacts stoichiometrically with acetone in the presence of acid to generate isopropanol. When a solution of **4**, generated from the addition of 10 equiv. of [DMFH][OTf] to **3**, was treated with 50 equiv. of acetone in C_6D_6, the disappearance of the Ir^{III}-H resonances of **4** was observed, accompanied by corresponding growth of isopropanol signals (Figure S7). These data reveal that while the hydride in **4** is unreactive to strong acid and is only mildly hydridic, it is nevertheless capable of reducing acetone to isopropanol, due to the cooperative activation of the carbonyl by the hydroxy group on the cyclopentadienyl ligand.

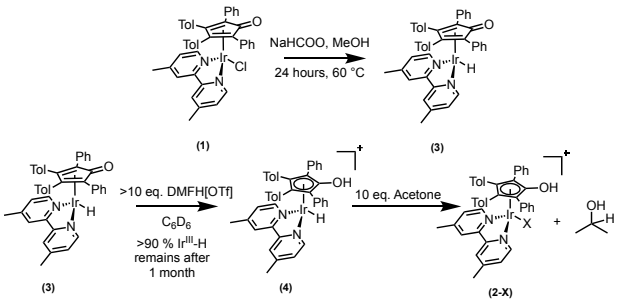


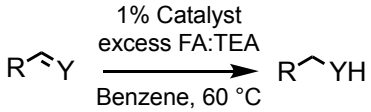
Figure 3. (top) Direct access to the Ir^{I}-H **(3)** by decarboxylative hydridation with sodium formate in methanol. **(bottom)** Treatment of Ir^{I}-H**, 3,** with DMFH[OTf] in C_6D_6 directly yields Ir^{III}-H, **4,** with negligible H_2 release. The resultant metal hydride is stable in the presence of excess acid for weeks, yet rapidly reacts with acetone to give stoichiometric isopropanol.

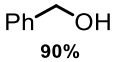
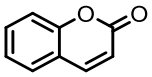
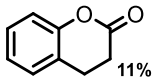
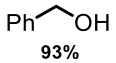
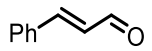
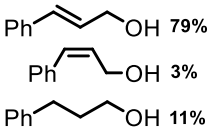
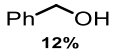
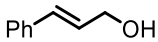
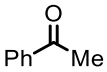
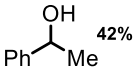
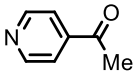
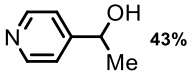
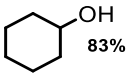
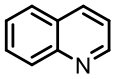
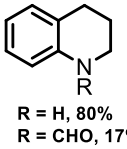
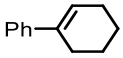
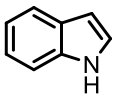
Catalytic Transfer Hydrogenation

To assess the catalytic competence of these Ir complexes, the transfer hydrogenation of a variety of unsaturated substrates was investigated with an azeotropic 5:2 formic acid : triethylamine mixture (FA:TEA)[22] in benzene at 60°C. Initial screening experiments were carried out with benzaldehyde as the substrate utilizing 1 mol% of the Ir cyclopentadienone complexes **1** and **3** as catalyst precursors. As shown in Table 2, both the Ir-Cl **1** and the Ir-H **3** performed comparably, affording benzyl alcohol in > 90% yield after 2 h (Table 2, entries 1 and 2). Subsequent experiments were carried out with the Ir-H **3** as the catalyst precursor (Table 2).

While catalysts derived from **3** exhibit good reactivity towards aldehydes under these conditions, ketones (Table 2, Entries 4 and 5) were reduced in lower yields and with longer reaction times. Unpolarized olefins were unreactive; 1-phenylcyclohexene was not hydrogenated (Table 2, Entry 6), but the more polarized alkene in coumarin was hydrogenated in low yield without any apparent reduction or ring-opening of the lactone (Table 2, Entry 7). This apparent preference for polarized C=C bonds over unpolarized ones is also evident in the hydrogenations of *trans*-cinnamaldehyde and *trans*-cinnamyl alcohol (Table 2, Entries 8-9). Transfer hydrogenation of *trans*-cinnamaldehyde yields *trans*-cinnamyl alcohol as the major product, with *cis*-cinnamyl alcohol and 3-phenylpropanol as minor side-products. Attempts to hydrogenate *trans*-cinnamyl alcohol led only to partial isomerization to *cis*-cinnamyl alcohol. This suggests that the 3-phenylpropanol observed in the transfer hydrogenation of *trans*-cinnamaldehyde results from C=C hydrogenation followed by C=O hydrogenation, and not the reverse process. These data are consistent with previous reports of Shvo-type transfer hydrogenations which are generally more selective for polarized functional groups.[4,9]

Table 2. Transfer Hydrogenation of Unsaturated Substrates with Ir-Shvo Complexes



Entry	Substrate	Products (yield)	Time (h)	Entry	Substrate	Products (yield)	Time (h)
1		 90%	2	7		 11%	24
2		 93%	2[a]	8		 79% 3% 11%	6
3		 12%	2[b]	9		 14%	6
4		 42%	24	10		 43%	24
5		 83%	24	11		 R = H, 80% R = CHO, 17%	24
6		No Reaction	24	12		No Reaction	24

Conditions: Catalyst **3** (3mM), substrate (320mM), FA:TEA (1.9M formic acid), benzene, 60 °C. [a]Catalyst **1** (3mM). [b]Catalyst **5** (3mM).

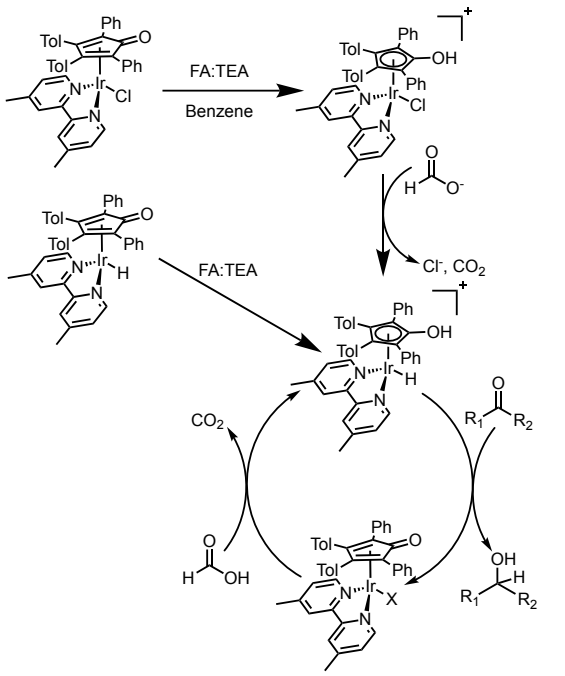


Figure 4. Proposed mechanism of transfer hydrogenation with formic acid. .

Nitrogen heterocycles were also examined. 4-acetylpyridine was hydrogenated to the corresponding secondary alcohol with no dearomatization (Table 2, Entry 10). Transfer hydrogenation of quinoline afforded 1,2,3,4-tetrahydroquinoline and the corresponding N-formylated product with high conversion after 24 hours (Table 2, Entry 11), but indole was unreactive under these conditions (Table 2, Entry 12). These differences are likely a consequence of the acidic conditions employed and the higher basicity of quinoline. As shown in Figure 4, we propose that the cationic hydroxycyclopentadienyl Ir-H is a key intermediate in the mechanism of transfer hydrogenation from the Ir-Cl or Ir-H precursors.

In view of the photoreactivity of related Cp*(bpy)IrH$^+$ complexes,[18,25,26] we sought to rule out photoactivation in the hydrogen transfer step of the mechanism proposed in Figure 4. When transfer hydrogenations of benzaldehyde (Table 2, entries 1-3) were carried out in vials wrapped in aluminum foil, we observed no meaningful difference between hydrogenations occurring under ambient illumination and those strictly protected from light.

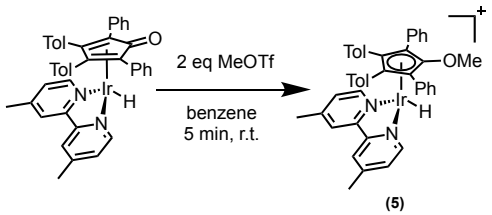


Figure 5. Synthesis of O-protected complex **5**

The observations that the acid-stable cationic Ir-H **4** reacts readily with acetone (Fig. 3) and the transfer hydrogenation activity of the cyclopentadienone complexes **1** and **3**, are consistent with a key role of the hydroxycyclopentadienyl group in the metal-ligand bifunctional activation[27] of carbonyl and heterocycle substrates. To further evaluate the role of the hydroxyclopentadienyl ligand, the O-methylated complex $[C_5Tol_2Ph_2OMe)(dmpby)(IrH]^+$ **5** was prepared by treating **3** with methyl triflate (Figure 5). The transfer hydrogenation of benzaldehyde with **5** (Table 2, Entry 3) reaches only 12% yield of benzyl alcohol in the same time that the analogous reaction catalyzed by **3** reaches 93% yield. Although catalysis is not completely inhibited by O-methylation, limiting the proton-transfer capacity of the cyclopentadienyl ligand significantly attenuates performance, strongly implicating metal-ligand cooperation in facilitating these hydrogenations.

Conclusion

We report a new class of cyclopentadienone and hydroxycyclopentadienyl Ir bpy complexes. The cationic Ir hydride $[(C_5Tol_2Ph_2OH)(dmpby)IrH]^+$exhibits similar acid stability of the analogous Cp* complexes $Cp^*(bpy)IrH^+$, but is able to reduce carbonyls under mild conditions due to the bifunctional cooperation of the hydroxycyclopentadienyl ligand. The cyclopentadienone complexes $(C_5Tol_2Ph_2O)(dmbpy)IrX$ (X = Cl, H) are competent precatalysts for transfer hydrogenation of carbonyls and heterocycles with ammonium formate in aromatic solvents and exhibit selectivity for polarized unsaturated substrates that is similar to related cyclopentadienone complexes of Ru, Fe, Re, and Mo. Mechanistic studies implicate the cationic Ir hydride $[(C_5Tol_2Ph_2OH)(dmpby)IrH]^+$ as a key intermediate in these catalytic transfer hydrogenation reactions.

Acknowledgements

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