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Activation and Deactivation of Cp*Ir(TsDPEN) Hydrogenation Catalysts in Water

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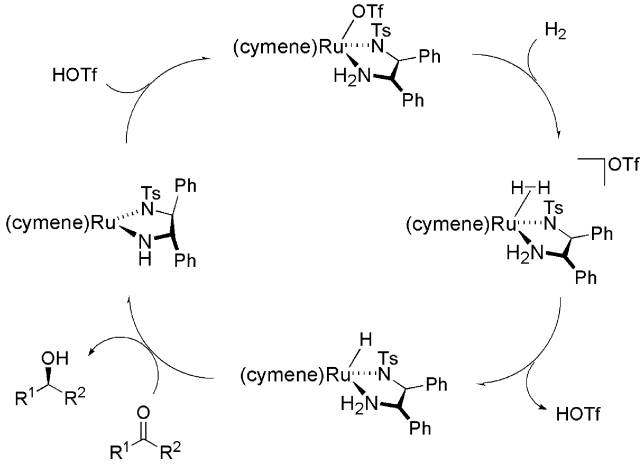
The addition of H_3PO_4 to Cp*Ir(TsDPEN-H), where TsDPEN = $H_2NCHPhCHPhNTs^-$, is a simple method to obtain a water-soluble hydrogenation catalyst capable of reducing aromatic ketones to their corresponding alcohols in aqueous solutions. Key to the reactivity is the low affinity of the coordinatively unsaturated $[Cp^*Ir(TsDPEN)]^+$ for $H_2PO_4^-$. Catalyst degradation proceeds via the protonation of the tosylamido ligand, as was established by the crystallographic characterization of the tosylamine complex $[Cp^*Ir(NCMe)(HTsDPEN)]^{2+}$.

Introduction

Numerous amine-supported hydrogenation catalysts have been reported in recent years, many being inspired by Ikariya and Noyori's pioneering work on transfer hydrogenation (TH) catalysis involving the (cymene)RuH(TsDPEN) motif, where TsDPEN = $H_2NCHPhCHPhNTs^-$.[1,2] These catalysts efficiently catalyze the transfer hydrogenation of polar substrates such as ketones from H_2-donors such as 2-propanol and formic acid[3] but are found to be minimally active in the presence of H_2.[2,4] Recently it was discovered that these amido complexes can be easily converted into catalysts for direct hydrogenation.[5–9]

The key insight is that protonation of 16e diamido complexes generates cationic derivatives that are sufficiently electrophilic to activate H_2 directly.[10,11] Upon exposure to H_2, these cationic complexes convert to amino hydrides that in turn reduce ketones and imines following the pathway for traditional TH catalysis (Scheme 1).[7,8,11] The new cationic catalysts offer significantly broadened flexibility to the hydrogenation of polar substrates. In specific examples, triflic acid (HOTf) converts (cymene)Ru(*S*,*S*-TsDPEN-H) and Cp*Ir(*S*,*S*-TsDPEN-H) into [(ring)M(*S*,*S*-TsDPEN)]OTf, which activates H_2 but will not abstract H_2 from traditional hydrogen donors.[8,9]



Scheme 1. Proposed mechanism for the catalytic hydrogenation of ketones by [(cymene)Ru(*S*,*S*-TsDPEN)]$^+$.

Results and Discussion

The present report is based from the following observation: addition of ca. 1 equiv. of H_3PO_4 to a two-phase CH_2Cl_2/H_2O solution containing Cp*Ir(TsDPEN-H) (**1**) causes the metal complex to transfer to the aqueous phase. The transfer of the iridium complex to the aqueous solution is indicated by the color change, consistent with the formation of $[Cp^*Ir(TsDPEN)]^+$ ($[\mathbf{1}H]H_2PO_4$) (Figure 1).[12] These observations are described by Equation (1).

$$Cp^*Ir(TsDPEN\text{-}H) + H_3PO_4 \rightarrow [Cp^*Ir(TsDPEN)]H_2PO_4 \quad (1)$$

The ^{31}P NMR spectrum of the D_2O solution of $[\mathbf{1}H]H_2PO_4$ indicated that the phosphate anion is non-coordinated, its chemical shift being identical to that seen for aqueous NaH_2PO_4 (δ = 0.87 for $[\mathbf{1}H]H_2PO_4$ vs. δ = 1.07 for NaH_2PO_4). The ^1H NMR spectrum is consistent with a five-coordinate complex, as indicated by the C*H*PhC*H*Ph signals that are diagnostic of *trans*-diaxial phenyl substitu-

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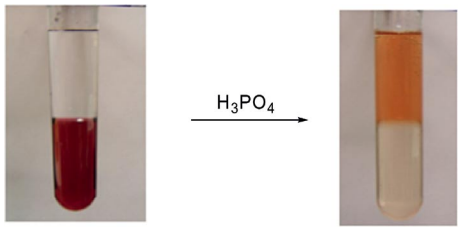


Figure 1. Solution of **1** in a 1:1 mixture of water and CH_2Cl_2 before (left) and after addition of one drop of H_3PO_4 (right).

ents. As we have reported,[10] [Cp*Ir(TsDPEN)]$^+$ tends not to bind oxyanions. When the reaction in Equation (1) was conducted in CH_2Cl_2/Et_2O solution, we obtained an orange precipitate that dissolved in water to give NMR spectra identical with those seen for the in-situ protonation. Elemental analysis indicates that this solid corresponds to [Cp*Ir(TsDPEN)]H_2PO_4·H_2O. As evidence for its coordinatively unsaturated character, [**1**H]H_2PO_4 was found to react in solution with CO and PMe_3 to rapidly give the adducts [**1**(CO)]$^+$ [ν_{CO} (KBr) = 2057 cm^{-1}] and [**1**(PMe_3)]$^+$ [δ (^{31}P, $CDCl_3$) = –28.09].[10,13] Analogous to the preparation of [**1**H]H_2PO_4, we generated [Cp*Ir(MsDPEN)]-H_2PO_4, [**2**H]H_2PO_4, by the reaction of H_3PO_4 with Cp*Ir(MsDPEN-H).[5] This salt is also catalytically active in water.

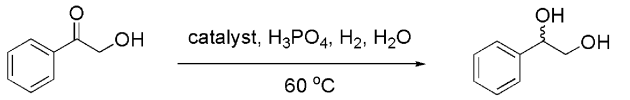
The hydrophilic nature of the $H_2PO_4^-$ is apparently critical to the water solubility of [**1**H]H_2PO_4, which contains an otherwise hydrophobic organometallic cation. For example, [Cp*Ir(TsDPEN)]OTf is insoluble in water. Sulfuric acid reacts with **1** to produce a bisulfate salt that is poorly water-soluble, indicating the diminished hydrophilicity of the HSO_4^- anion. Nitric acid also does not afford a water-soluble salt. Although (cymene)Ru(TsDPEN-H) reacts with H_3PO_4, the resulting product proved insoluble in water. It is known, however, that the [(cymene)Ru(TsDPEN)]$^+$ center is more Lewis acidic than the related [Cp*Ir(TsDPEN)]$^+$.[12] Thus [(cymene)Ru(TsDPEN)H_2PO_4], [**3**H(H_2PO_4)], is probably non-ionic. Severin and co-workers have previously shown that phosphonates bind to [(arene)Ru(diamine)]$^+$ centers.[14]

[**1**H]H_2PO_4 catalyzes the hydrogenation of 2-hydroxyacetophenone (ACP-2-OH) in aqueous solutions (Table 1). In a typical procedure, a suspension of 4 mg of **1** in 1 mL of H_2O is treated with 1.1 equiv. of H_3PO_4 to afford a homogeneous red-orange solution. The solution is added to a suspension of 200 mg of ACP-2-OH in 4 mL of water and pressurized with 10 atm of H_2. Catalytic hydrogenation of ACP-2-OH employing *S*,*S*-[**1**H]H_2PO_4 afforded the (*R*)-diol with an *ee* of 75%, thereby establishing the integrity of the Ir-DPEN ensemble during catalysis.

The pH of a completed hydrogenation reaction was found to be 3. When the reaction solution was buffered to pH 6 using NaH_2PO_4/Na_2HPO_4, the rate was only marginally affected. Catalysis was also observed in MeOH, but conversions were higher in pure aqueous solution (Table 2).

Catalyst [**1**H]H_2PO_4 degrades as evidenced by decreased TOF concomitant with the bleaching of the solution color.

Table 1. Aqueous hydrogenation experiments.[a]



Catalyst	Time [h]	S/C	TON[b]	TOF [h^{-1}]	Conversion [%]	Notes
[**1**H]H_2PO_4	6	250	150	25	60	
[**1**H]H_2PO_4	6	250	202	34	81	[c]
[**1**H]H_2PO_4	14	250	225	16	90	
[**1**H]H_2PO_4	12	1000	650	54	65	[d,e]
[**1**H]H_2PO_4	6	250	175	29	70	[f]
[**1**H]H_2PO_4	12	1000	0	0	0	[g]
[**1**H]H_2PO_4	6	250	200	33	80	[h]
[**1**H]H_2PO_4	18	200	0	0	0	[i]
[**2**H]H_2PO_4	12	1000	590	49	59	[d,e]
[**3**H(H_2PO_4)]	24	200	0	0	0	[d,e]

[a] Unless otherwise noted, reactions were conducted with [**1**H]-H_2PO_4 developed in situ using **1** and 1.1 equiv. H_3PO_4, along with 1.5 mmol of 2-hydroxyacetophenone and 5 mL H_2O in a glass autoclave pressurized with 10 atm H_2. [b] Determined by ^{1}H NMR spectroscopy. [c] Using isolated [**1**H]H_2PO_4. [d] Performed in a stainless steel autoclave. [e] Pressure: 30 atm. [f] Temperature: 40 °C. [g] Employing 200 equiv. of H_3PO_4. [h] pH = 6, NaH_2PO_4 buffer solution was employed. [i] DMSO employed as solvent.

Table 2. Effect of water/methanol ratio on hydrogenation of 2-hydroxyacetophenone by [**1**H]H_2PO_4.[a]

MeOH [mL]	H_2O [mL]	Conversion [%][b]
5	0	35
2.5	2.5	58
0	5	70

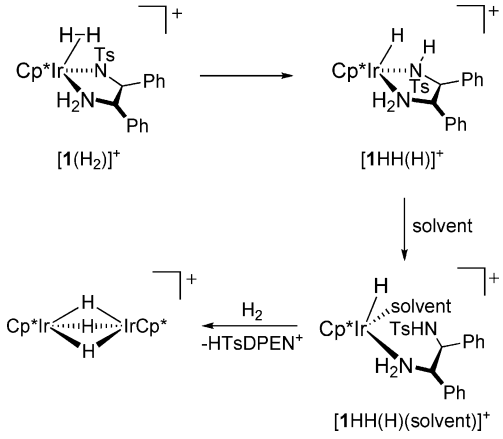
[a] Reactions were performed for 6 h at 40 °C under 10 atm of H_2 in a glass autoclave. [b] Determined by ^{1}H NMR spectroscopy.

The degradation product, [Cp*$_2$Ir$_2$(μ-H)$_3$]$^+$,[15] was independently generated by treating an aqueous solution of [**1**H]-H_2PO_4 with 10 atm of H_2 at 60 °C. Also formed in this hydrogenolysis is HTsDPEN$^+$. We found that [Cp*$_2$Ir$_2$(μ-H)$_3$]H_2PO_4 hydrogenates ACP-2-OH to the diol, but it is a relatively poor catalyst.

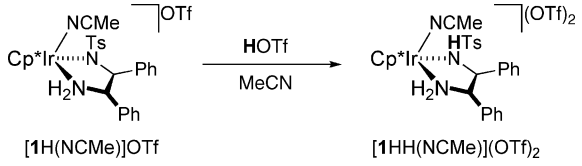
We propose that the degradation of [**1**H]H_2PO_4 is initiated by intramolecular proton transfer from a dihydrogen ligand to the tosylamido nitrogen, which is usually considered nonbasic (Scheme 2).[16] The hydrogenolytic deactivation of [**1**H]$^+$ may be generally applicable to amido-based TH catalysts under acidic conditions.

Protonation of the TsDPEN ligand would weaken the Ir-NTs bond. Xiao and co-workers have proposed that the TsDPEN ligand becomes hemi-labile under acidic conditions and have isolated [(cymene)Ru(dppe)(κ^1-TsDPEN)]$^{2+}$, wherein the tosylamine (RNHTs) is pendant by virtue of the bidentate nature of dppe.[17b] The ability of tosylamines to coordinate to these soft metal centers remains unproven.

We found that treatment of the acetonitrile adduct [**1**H(MeCN)]$^+$ with HOTf afforded a salt containing the proposed tosylamino ligand [Equation (2)].[17] The soft MeCN ligand enhances the basicity of the dicationic Ir site.



Scheme 2. Proposed catalyst deactivation mechanism.



(2)

Single crystals suitable for X-ray crystallography of $[Cp^*Ir(MeCN)(HTsDPEN)]^{2+}$, $[\mathbf{1}HH(NCMe)](OTf)_2$, were isolated as the OTf^- salt and were analyzed (Figure 2).

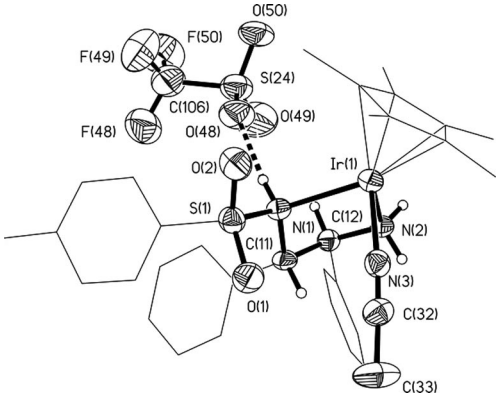


Figure 2. Molecular structure showing [Cp*Ir(NCMe)(HTsDPEN)](OTf)$_2$. The thermal ellipsoids are drawn at 50% probability and are omitted on the Cp* and phenyl groups for clarity.

The crystallographic analysis shows that all Ir–ligand bonds in the dication are elongated relative to the conjugate base $[\mathbf{1}H(NCMe)]^+$.[10] The ca. 0.1 Å elongation of the *Ir–N*HTs bond is striking. One triflate anion hydrogen-bonds (r_{N-O} = 2.876 Å) to the N*H*Ts (Figure 1) (see Supporting Information). In this dicationic MeCN adduct, the phenyl groups are diequatorial as observed in related pseudo-octahedral complexes.

To determine the relative acidity of the tosylamine, pK_a measurements were undertaken in MeCN. Using urea as a base (pK_a = 7.7 in MeCN),[18] the tosylamine proton was found to have a pK_a of 8.55 ± 0.32, which is 13 orders of magnitude more acidic than the NH_2 proton of $[\mathbf{1}H]^+$.[11] Using the correlations of pK_a's of pyridines in other solvents, the pK_a of the tosylamine proton of $[\mathbf{1}HH(NCMe)]^{2+}$ can be estimated to be fairly acidic at 1.77 in H_2O and 2.12 in MeOH, with the pK_a being about two pK_a units lower for $[\mathbf{1}HH]^{2+}$.[19] The lability of the HTsDPEN ligand in the unsaturated $[\mathbf{1}HH]^{2+}$ is attributed to the high acidity of the dicationic tosylamine complex.

Conclusions

The present report further demonstrates the versatile behavior of the soft Lewis acid $[\mathbf{1}H]^+$, which is now suitable for studies in aqueous solution. The work also clarifies the degradation pathway of this emerging class[20] of cationic catalysts.

Experimental Section

$[Cp^*Ir(TsDPEN)]H_2PO_4{\cdot}H_2O$ $[\mathbf{1}H]H_2PO_4$: Cp*Ir(TsDPEN-H) (250 mg, 0.36 mmol) was dissolved in a mixture of CH_2Cl_2 (5 mL) and Et_2O (50 mL). An aqueous solution of H_3PO_4 (25 μL, 85%) was added to the red-orange solution to afford a light orange precipitate. The precipitate was isolated via filtration to afford a light orange solid (205 mg, 72%). ^1H NMR (500 MHz, D_2O): δ = 1.72 (s, 15 H, Cp*), 2.14 (s, 3 H, $SO_2C_6H_4$-4-C*H*$_3$), 4.20 (br. s, 1 H, $H_2NCHPhCHPhNTs$), 4.44 (br. s, 1 H, $H_2NCHPhCHPhNTs$), 6.78–7.31 (14 H, aromatic) ppm. ^1H NMR (500 MHz, CD_3OD): δ = 1.90 (s, 15 H, Cp*), 2.27 (s, 3 H, $SO_2C_6H_4$-4-C*H*$_3$), 4.09 (d, J = 3.8 Hz, 1 H, $H_2NCHPhCHPhNTs$), 4.59 (d, J = 3.8 Hz, 1 H, $H_2NCHPhCHPhNTs$), 6.88–7.24 (14 H, aromatic) ppm. ^{13}C (125 MHz, CD_3OD): δ = 5.41, 16.47, 65.69, 71.85, 85.80, 122.98, 123.48, 123.69, 123.72, 124.12, 124.32, 124.56, 125.17, 134.20, 136.42, 138.60 ppm. ^{31}P NMR (500 MHz, D_2O): δ = 1.00 (s) ppm. ^{31}P NMR (500 MHz, CD_3OD): δ = 2.21 (s) ppm. $IrC_{31}H_{40}N_2O_7PS{\cdot}H_2O$ (807.91): calcd. C 46.09, H 4.99, N 3.47; found C 45.83, H 4.67, N 3.39.

$[Cp^*Ir(NCMe)(HTsDPEN)](OTf)_2$ $[\mathbf{1}HH(NCMe)](OTf)_2$: A CH_2Cl_2 solution of (100 mg, 145 μmol) Cp*Ir(TsDPEN-H) was treated with (40 μL, 450 μmol) of triflic acid resulting in an immediate color change from reddish-purple to a bright yellow color. The solution was stirred for 30 min, and the solvent was removed under reduced pressure. A yellow slightly oily solid was obtained and washed with *n*-hexane. No further work up was attempted due to the extreme instability of the complex, which resulted in [Cp*Ir(TsDPEN)]OTf upon exposure to Et_2O or THF. Exposure of the solid to air longer than 24 hours resulted in a slight discoloration to a reddish-orange color indicative of formation of [Cp*Ir(TsDPEN)]OTf. ^1H NMR (500 MHz, CD_3CN): δ = 1.60 (s, 15 H, Cp*), 2.28 (s, 3 H, $SO_2C_6H_4$-4-C*H*$_3$), 4.11 (t, J = 10 Hz, 1 H, $H_2NCHPhCHPhNHTs$), 4.52 (t, J = 10 Hz, 1 H, $H_2NCHPhCHPhNHTs$), 4.73 (br. t, J = 10 Hz, 1 H, $HNCHPhCHPhNHTs$), 5.49 (br. d, J = 10 Hz, 1 H, $HNCHPhCHPhNHTs$), 6.73–7.52 (m, 14H and $H_2NCHPhCHPhNHTs$) ppm.

Procedure for Hydrogenation of 2-Hydroxyacetophenone: Cp*Ir(TsDPEN-H) (4 mg, 5.8 μmol) was suspended in deionized water (1 mL), followed by the addition of an aqueous solution of H_3PO_4 (25 μL, 0.29 M). Vigorous shaking of the suspension afforded a red-orange solution, which was transferred into a 80 mL silated glass autoclave along with 2-hydroxyacetophenone (200 mg, 1.47 mmol), deionized H_2O (4 mL), and a magnetic stir bar. The autoclave was pressurized with 14 atm H_2 and depressurized to

5 atm in three cycles before reaching a final H_2 pressure of 10 atm. The autoclave was heated to 60 °C and its contents were stirred vigorously for 12 h. Product ratios were identified via ^1H NMR spectroscopy ($CDCl_3$) of the solid obtained upon removal of H_2O.

Supporting Information (see also the footnote on the first page of this article): Molecular structure data of [Cp*Ir(NCMe)(HTsDPEN)](OTf)$_2$ and [TsDPENH]OTf, synthetic preparations, HPLC traces and other spectroscopic data.

CCDC-743230 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgments

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