

Imination Catalysis via Two-point Binding of Substrate Aldehyde via a Metal and a Pendant Hydrogen-Bonding Group

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Imination of carbonyl compounds is important in heterocycle synthesis and in the biosynthesis of amino acids^{1,2} but side reactions can occur, such as amination. Both base³ and acid catalysts (e.g., ZnCl₂)⁴ are known but these tend to be unselective. Eisch and Sanchez have reported a useful aluminum complex capable of selectively catalyzing imination.¹

Our interest in metal complexes with pendant hydrogen bonding groups led us to test [(bq-NH₂)IrH(H₂O)(PPh₃)₂](BF₄) (**1**) (bq-NH₂ = 2-aminobezoquinolate)⁵ for catalytic imination. Since we expected the aldehyde reagent but not the imine product to bind to the metal, selectivity for imine formation seemed likely. In this study *p*-tolualdehyde (*p*-ArCHO) is indeed found to bind to **1** to give a crystalline derivative, [(bq-NH₂)IrH(*p*-ArCHO)(PPh₃)₂](BF₄) (**2**) (Scheme 1), and imine formation from *p*-ArCHO and MesNH₂ (2,4,6-trimethylphenylamine) is catalyzed by complexes **1** and **2**.

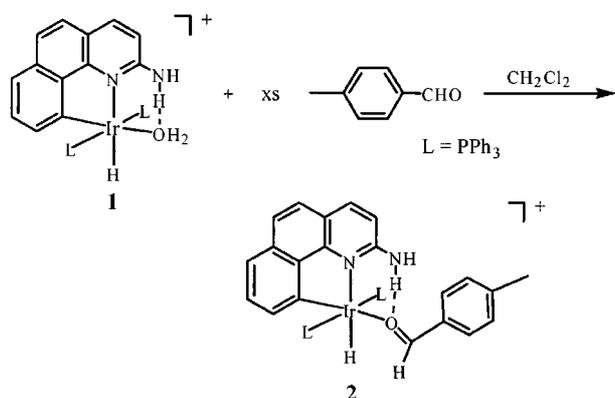
The complex **2** was obtained by the reaction of **1** with excess *p*-ArCHO in CH₂Cl₂ (Scheme 1). Crystallization of **2** from dichloromethane/hexane yields single crystals suitable for X-ray structure determination. A summary of crystal parameters and refinement results is given in Table 1 and selected bond lengths and angles are compiled in Table 2. The ORTEP view of the cationic portion of the complex is depicted in Figure 1. The most important feature of **2** is that the pendant NH₂ group is capable of hydrogen bonding to the carbonyl oxygen atom of the aldehyde. Although the NH₂ hydrogens are not observed, the N-O distance of 2.86 Å is consistent with an N-H...O hydrogen bond.⁶ Two

distinctive ν(NH) IR bands at 3359 and 3471 cm⁻¹, shifted from the free ligand band at 3411 cm⁻¹, also indicate hydrogen bonding. In the ¹H NMR spectrum at low temperature (below -40 °C), the H-bonded NH is observed at 7.70 ppm, whereas the non-hydrogen-bonded NH is observed at 5.85 ppm.

We examined catalytic imination of *p*-ArCHO with MesNH₂ in the presence of complexes **1** or **2**. When equivalent amounts of *p*-ArCHO and MesNH₂ were treated with 5 mol% **1** or **2** at 25 °C in CD₂Cl₂ in an NMR tube (Scheme 2), we found an average rate of 18 turnovers/hr.

Control reactions without catalyst or with an NH₃ ligand, **3**, blocking the *p*-ArCHO binding site, showed that no detectable amount of imine was formed. Therefore, binding of an aldehyde to the iridium ion seems essential for the imine formation.

We next tested the catalytic imination of *p*-tolualdehyde with an analogous iridium complex, **4**,⁷ lacking a pendant NH₂ group. The aqua ligand in **4** could be easily replaced by



Scheme 1

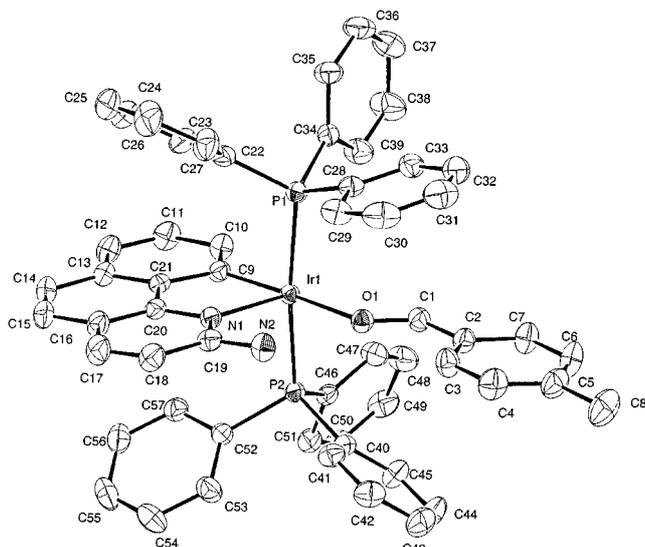
Table 1. Crystallographic data for **2**·CH₂Cl₂

Formula	C ₅₈ H ₅₀ N ₂ OBF ₄ P ₂ Cl ₂ Ir
MW	1202.92
Temperature, K	183
Crystal system	triclinic
Space group	P ₁ (#2)
a (Å)	10.1501(2)
b (Å)	13.0430(3)
c (Å)	20.7801(5)
α (degree)	96.911(1)
β (degree)	97.014(1)
γ (degree)	109.373(1)
V, Å ³	2537.5(1)
F(000)	1204.00
Z	2
Calculated density, g/cm ³	1.574
λ(Mo Kα), Å	0.71069
Scan type	ω-2θ
Reflections measured/unique	22080/14888 [R _{int} = 0.036]
R ^a	0.033
R _w ^b	0.042
Goodness of fit indicator	1.44

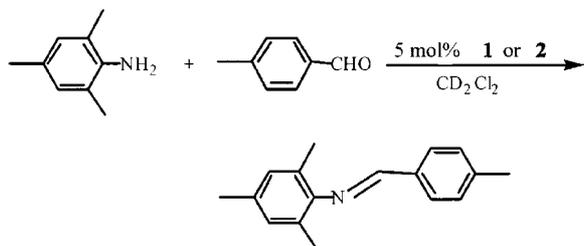
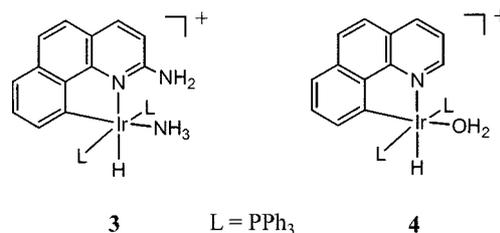
^aR = Σ||F_o - |F_c|| / Σ|F_o|, ^bR_w = [(Σw(|F_o - |F_c||)² / ΣwF_o²]^{1/2}

Table 2. Selected bond distances (Å) and bond angles (°) of 2-CH₂Cl₂

Bond lengths			
Ir(1)-P(1)	2.3203(7)	Ir(1)-O(1)	2.197(2)
Ir(1)-C(9)	2.013(3)	Ir(1)-P(2)	2.345(7)
Ir(1)-N(1)	2.203(2)	O(1)-C(1)	1.241(4)
Bond angles			
P(1)-Ir(1)-P(2)	170.29(2)	P(1)-Ir(1)-N(1)	95.20(7)
P(1)-Ir(1)-O(1)	90.71(6)	P(1)-Ir(1)-C(9)	89.94(8)
P(2)-Ir(1)-O(1)	89.77(6)	P(2)-Ir(1)-C(9)	90.14(8)
P(2)-Ir(1)-N(1)	94.37(6)	O(1)-Ir(1)-C(9)	176.60(9)
O(1)-Ir(1)-N(1)	96.66(8)	N(1)-Ir(1)-C(9)	80.0(1)
Ir(1)-P(1)-C(22)	115.69(10)	Ir(1)-P(1)-C(34)	118.3(1)
Ir(1)-P(1)-C(28)	109.60(9)	Ir(1)-P(2)-C(40)	112.7(1)
Ir(1)-P(2)-C(52)	116.57(10)	Ir(1)-P(2)-C(46)	116.09(9)
Ir(1)-O(1)-C(1)	126.5(2)	Ir(1)-N(1)-C(19)	130.2(2)
Ir(1)-N(1)-C(20)	111.1(2)	Ir(1)-C(9)-C(21)	114.5(2)
Ir(1)-C(9)-C(10)	128.9(2)		

**Figure 1.** ORTEP view of the cationic portion of 2-CH₂Cl₂ (50% ellipsoids).

p-tolualdehyde and the spectroscopic data of the resulting compound revealed that the carbonyl oxygen atom of the aldehyde was bound to the iridium ion. However, the rate of catalytic imine formation for *p*-tolualdehyde with MesNH₂ was only 14 turnovers/hr with the catalyst **4**, small but significant rate decrease in comparison with the complex **1**.

**Scheme 2**

Therefore, the presence of the H-bonding group in **1** seems to be responsible for the enhanced catalytic activity. Another control studies was performed with mesitaldehyde (2,4,6-trimethylbenzaldehyde). We expected the two bulky methyl groups at the 2- and 6- carbon positions in the phenyl ring to prevent the aldehyde group from H-bonding to the pendant NH₂ in **1**, due to steric repulsion between the methyl groups and the NH₂. This was, indeed, confirmed by NMR and IR spectroscopic studies, showing no interaction between the N-H and C=O groups in the complex generated (*in situ*) from the reaction of mesitaldehyde and **1**. As expected, the mesitaldehyde imination of MesNH₂ with the catalyst **1** resulted in no improvement at all in catalytic activity (6 turnovers/hr), in comparison with the catalyst **4** (6 turnovers/hr).

In summary a small enhancement in catalytic activity has been achieved *via* two-point binding of substrate aldehyde. Several interesting catalytic reactions have been suggested to proceed *via* a pathway involving cooperative coordination of a carbonyl group by two Lewis acidic metal centers.^{8,9} Our studies, however, represents the first time a carbonyl has been activated in a two-point fashion via a coordinate metal-O bond and an N-H···O hydrogen bond, as far as we know. The relatively modest rate increase for **1** or **2** vs. **4** may indicate that hydrogen bonding stabilizes the transition state (ts) only slightly more than it does the ArCHO complex (the ground state). Selective stabilization of the ts is required for significant catalytic acceleration by hydrogen bonding. There must therefore be a subtle mismatch between the hydrogen bonding pendant group to give weak binding in the ground state but a match in the ts. Further study will focus on the effects of a pendant hydrogen-bonding group on homogeneous catalysis for other important organic reactions.

Experimental Section

Reagents and solvents were of commercially available reagent quality. Preparation and handling of Ir complexes were carried out under argon with standard Schlenk techniques. ¹H NMR spectra were measured in CDCl₃ or CD₂Cl₂ on a Bruker (300 MHz) NMR spectrometer. Infrared spectra were recorded neat or in Nujol mulls on a Mattson Galaxy 4030 FT-IR spectrometer.

[(bq-NH₂)IrH(*p*-ArCHO)(PPh₃)₂](BF₄) (**2**). [(bq-NH₂)IrH-(H₂O)(PPh₃)₂](BF₄) (**1**) (0.4 g, 0.39 mmol) was dissolved in 10 mL of degassed CH₂Cl₂ under Ar in a Schlenk flask. To the clear yellow solution was added *p*-tolualdehyde (0.4 g,

3.3 mmol) and the resulting mixture was stirred at room temperature for 20 min. A mixture of hexane/diethyl ether (50/50) was added until the solution became cloudy. The solution was filtered and more hexane/diethyl ether was added to precipitate yellow crystalline solid. The solid was collected by filtration, washed with diethyl ether. The product was recrystallized in $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ and dried *in vacuo*. Yield: 0.32 g (75%). ^1H NMR (CD_2Cl_2 , 300 MHz, 293K, ppm): δ -16.18 (t, 1H, $^2J_{\text{HP}} = 14.6$ Hz, Ir-H), 2.38 (s, 3H, $-\text{CH}_3$), 6.36 (br, s, 1H, N-H), 6.60-7.42 (m, 42H), 9.98 (br, s, CHO). $^{31}\text{P}\{^1\text{H}\}$ NMR (CD_2Cl_2 , 125 MHz, 293K, ppm) δ 20.3 (s). IR (thin-film, cm^{-1}): ν , 1595 (C=O), 2197 (Ir-H), 3359 (NH), 3471 (NH). Anal. Calc. for $\text{C}_{57}\text{H}_{48}\text{N}_2\text{OBF}_4\text{P}_2\text{Ir}$: C, 61.20; H, 4.29; N, 2.51. Found: C, 61.62; H, 4.32; N, 2.36.

X-ray Crystallography. A yellow column crystal of $2 \cdot \text{CH}_2\text{Cl}_2$ having approximate dimensions of $0.12 \times 0.12 \times 0.20$ mm was mounted on a glass fiber. All measurements were made on a Nonius KappaCCD diffractometer with graphite monochromated Mo-K α radiation. Cell constants and an orientation matrix for data collection were obtained from least-squares refinement, using ten (1° in ω , 10s exposure, de-zingered) data frames. The data were collected at a temperature of -90°C to a maximum 2θ value of 61.0° . Of the 22080 reflections that were collected, 14888 were unique ($R_{\text{int}} = 0.036$); equivalent reflections were merged. No decay correction was applied. The linear absorption coefficient, μ , for Mo-K α radiation is 28.6 cm^{-1} and a SORTAV¹⁰ absorption correction was applied. The data were corrected for Lorentz and polarization effects. The structure was solved by heavy-atom Patterson method and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The NH_2 hydrogens were included in difference map positions, but not refined. The Ir-H was not observed in the difference map. A summary of crystal parameters and refinement results is given in Table 1. Crystallographic data for the structure reported here have been deposited with the Cambridge

Crystallographic Data Centre (Deposition No. CCDC-183971). The data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html> (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk)

Catalytic Turnover Measurement. Typically, equimolar (0.3 mmol) ArCHO and MesNH_2 were placed in a NMR tube containing CD_2Cl_2 (0.6 mL) with 5 mol % catalyst (15 mol). Imine formation was followed by the disappearance of the $-\text{CH}=\text{O}$ resonance at 9.98 ppm and the appearance of the imine $-\text{CH}=\text{N}$ resonance at 8.16 ppm. All reactions were run at least in triplicate and the data reported represent the average of these reactions.

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