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The synthesis and catalytic activity of the iridium(I) hydroquinone complex $[(H_2Q)Ir(COD)]^+$

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ABSTRACT

The η^6-hydroquinone iridium complex $[(\eta^6\text{-}H_2Q)Ir(COD)]BF_4$ undergoes facile double deprotonation to the η^4-quinone anionic analogue. The latter has been shown to be the first example of an iridium complex that catalyzes 1,4 conjugate addition reactions of aryl boronic acids to electron deficient olefins.
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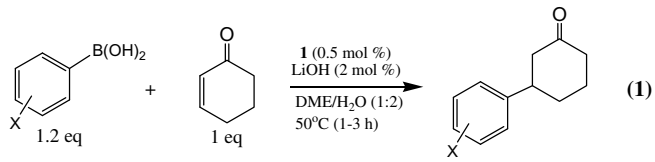
1. Introduction

We have recently shown that the rhodium(I) hydroquinone complex $[(\eta^6\text{-}H_2Q)Rh(COD)]^+$ (**1**) serves as an excellent catalyst precursor for the 1,2-addition of aryl boronic acids to aldehydes and the 1,4 conjugate addition to electron deficient alkenes [1,2]. The active catalyst in these reactions, which can be conducted in an aqueous medium, is believed to be the anionic η^4-quinonoid complex $[(\eta^4\text{-}Q)Rh(COD)]^-$ (**2** in Scheme 1). Complex **2** is readily formed from **1** by deprotonation and has been structurally characterized with the cationic counterions Li^+, K^+, and Bu_4N^+ [1,3]. The conjugate additions, typified by the reaction of 2-cyclohexen-1-one shown in Eq. (1), generally give high yields, even with very electron deficient aryl boronic acids, and occur with minimal proto-deborylation and without formation of any Heck products.

The impressive results found with **1** as a catalyst precursor prompted us to examine the chemistry of the iridium analogue, $[(\eta^6\text{-}H_2Q)Ir(COD)]^+$ (**3**). The more than tenfold lower cost of iridium in comparison to rhodium provides strong motivation for this work. Iridium complexes are perhaps best known in catalytic hydrogenations [4], can also be useful in catalytic C–C and C–X (X = N, O, B) bond formation in allylic alkylation, cycloaddition, and alkyne trimerization reactions, etc. [5]. Iridium-catalyzed conjugate addition of aryl boronic acids has been shown to occur with electron deficient di-enones to give 1,6-adducts regiospecifically in the presence of $[Ir(COD)(OH)]_2$ [6]. However, no products of addition to enones (e.g., Eq. (1)) or of 1,4-addition to di-enones were found with $[Ir(COD)(OH)]_2$. In striking contrast to this behavior, the rhodium analogue $[Rh(COD)(OH)]_2$ was shown to catalyze addition to both enones and di-enones, with a preference for the former electrophiles. Rhodium-catalyzed addition to di-enones was found to be poorly regioselective, yielding a mixture of 1,4- and 1,6-adducts [6]



(1)

Herein we report the synthesis of $[(\eta^6\text{-}H_2Q)Ir(COD)]^+$ (**3**) and demonstrate that it can indeed function as a catalyst precursor for the 1,4-addition of aryl boronic acids to the electron deficient olefin 2-cyclohexen-1-one, in analogy to the reaction shown in Eq. (1). It is also disclosed that facile deprotonation of the hydroquinone ligand in **3** with a metal alkoxide allows the formation of heterogeneous self-supporting quinonoid coordination networks and allows the covalent attachment of the iridium quinonoid complex to silica surfaces. It should be noted that the synthesis of iridium quinonoid complexes based on the fragment $Ir(Cp^*)^{2+}$ has been reported previously, but without any applications [7].

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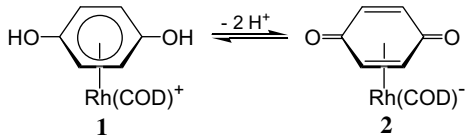


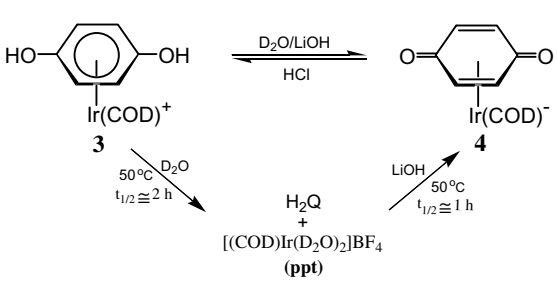
Scheme 1.

2. Results and discussion

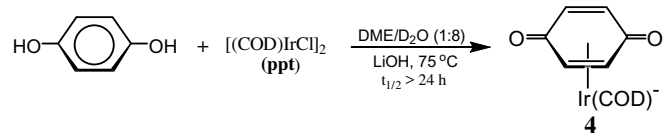
The iridium hydroquinone complex [3]BF_4 was easily synthesized as an air-stable solid by reaction of commercially available $[Ir(COD)Cl]_2$ with $AgBF_4$ and subsequent treatment with hydroquinone. ^{1}H NMR spectra show that **3** is rapidly and reversibly deprotonated by two equivalents of LiOH in D_2O to afford the anionic quinone complex **4**, which was found to be unchanged in this solvent after 20 h at 75 °C. While stable indefinitely in CH_2Cl_2, complex **3** in D_2O at 50 °C is slowly attacked by the solvent to liberate hydroquinone and generate the insoluble $[(COD)Ir(D_2O)_2]BF_4$ according to Scheme 2. Interestingly, subsequent addition of LiOH to the reaction mixture was found to result in the slow recoordination of the hydroquinone dianion to the iridium to generate the quinone complex **4**. In related experiments, the formation of **4** from the reaction of hydroquinone with insoluble $[(COD)IrCl]_2$ in a basic aqueous medium according to Scheme 3 was attempted, but only small amounts of product were generated after 20 h at 75 °C.

Our initial catalysis work focused substituting the iridium hydroquinone complex **3** for the rhodium complex **1** in 1,4 conjugate addition to 2-cyclohexen-1-one using reaction conditions outlined in a previous publication, which consisted of 0.5 mol% of the catalyst, 1.2 equivalents of boronic acid in DME and water [1,2]. While these conditions yielded no measurable product at 50 °C, when the temperature was increased to 75 °C the desired product was isolated in 29% yield. Although this discovery is noteworthy in that it is the first example of an iridium catalyzed 1,4 conjugate addition reaction, the isolated yield is well below practical limits for the reaction. By comparison, rhodium(I) species catalyze the reaction with the same starting materials in over 95% yield in less than 3 h, leaving a great deal of improvement for the iridium catalyst system.

After the original DME/water solvent system failed to produce reasonable yields, a number of solvent combinations were screened to find the best conditions for the iridium complex **3** (Table 1). During this process several key differences between the iridium **3** and rhodium **1** were observed. First of all, if the proton source of the reaction was changed from water to an alcohol, such as methanol or ethanol, the reactivity of the iridium complex decreased significantly. When rhodium (**1**) was used as the catalyst, these changes had little to no effect on the overall yield of the reaction. Second, ethereal solvents, which were the standard organic co-solvents used for the rhodium catalyzed 1,4-addition reactions,

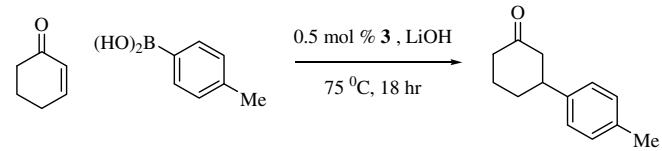


Scheme 2.



Scheme 3.

Table 1
Solvent study of 1,4 conjugate additions catalyzed by **4**.



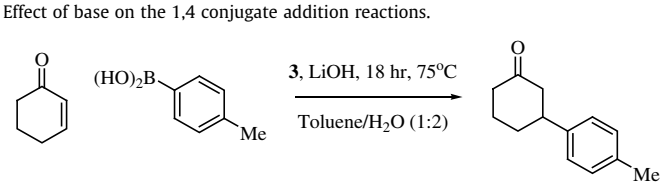
Entry	Solvent system	% Yield	Entry	Solvent system	% Yield
1	DME/water (1:2)	29	5	EtOH	0
2	THF/water (1:2)	18	6	MeOH	0
3	Dioxane/water (1:2)	0	7	MeOH/water (1:2)	10
4	Water	26	8	Toluene/water (1:2)	36

did not work well for the iridium complex **3**, which never produced yields higher than 30%, even when 5 mol% of catalyst was used. Although water was determined to be one of the better co-solvents, reactions carried out in pure water with no organic co-solvent gave only 26% yield.

With low catalyst loading, water and toluene appeared to offer the best chance at improving the yield of reactions catalyzed by the iridium complex based on its ability to solubilize the boronic acid and maintain catalytic activity, in relation to the other solvents. Conditions used were similar to the DME/water reaction, and the desired product was isolated in 36% yield. A number of variables were altered in an attempt to increase the isolated yield to levels obtained using the rhodium catalyst system. First, the catalyst loading was increased to 1 mol% and the amount of base was varied to measure its effects on the reaction (Table 2). It was found that small changes in the amount of base added, varying from 4 to 10 equivalents, had no visible effect on the catalyst or the reaction in general, but when 200-fold excess base was used the yield dropped by two thirds to 11%.

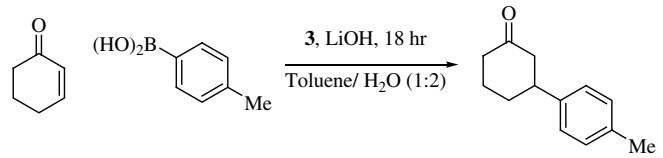
Since the concentration of base seemed to play a limited role in determining the catalytic ability of the iridium catalyst **3**, other possible factors were examined, including catalyst loading, equivalents of boronic acid and temperature (Table 3). Results showed

Table 2
Effect of base on the 1,4 conjugate addition reactions.



Entry	Mol% catalyst	Mol% base	% Yield
1	0.5	2	36
2	1	4	35
3	1	6	31
4	1	10	33
5	1	200	11

Table 3
Effect of several variables on the catalytic ability of **4**.



Entry	Mol% catalyst	Boronic acid (Eq)	Temperature (°C)	Yield
1	1	2	75	36
2	1	2	60	17
3	1	2	90	48
4	1	2.5	90	53
5	1	3	75	50
6	2	3	75	66
7	3	3	75	69
8	4	3	75	62
9	5	2	75	55
10	5	3	75	66
11	5	3	90	53
12	5	3	80	53

that lower temperatures hindered the catalyst's ability to promote the conjugate addition reaction, while increasing the temperature to 90 °C improved the overall yield to 48% (Table 3, entry 3). With the addition of greater amounts of boronic acid came further improvements in yield, including 50% at 75 °C and 1 mol% catalyst (entry 5). While all these results demonstrated significant improvements, the iridium complex **3** was unable to produce results similar to those obtained using the rhodium catalyst. Finally, the catalyst loading was varied between 1 mol% and 5 mol%, but yields failed to increase appreciably with the amount of catalyst added. Although no significant variation was observed between 2 mol% and 5 mol% catalyst loading, 3 mol% was selected as the "optimal" conditions as it gave the desired product in 69% yield (entry 7). Further attempts to improve yield by increasing the reaction temperature to 90 °C failed to produce useful results, and, in fact, the yield decreased compared to reactions run at 75 °C. We attempted to find a slightly higher temperature where the increased catalyst loading might have an advantageous effect, but even at 80 °C no appreciable improvements were observed.

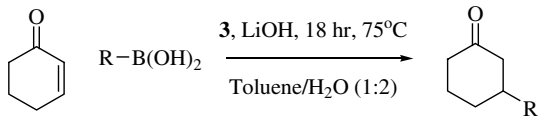
To conclude our study of the iridium hydroquinone catalyst system a number of different substrates were tried in an attempt to establish the generality of the catalyst. A variety of different boronic acids were subjected to the reaction conditions, and while it was found that *o*-tolylboronic acid reacted in similar yield to *p*-tolylboronic acid, while the other boronic acids either gave extremely poor yields, or did not react at all (Table 4). When different conjugate acceptors were tested similar results were obtained, with most not reacting at all (Table 5). The lone exception, ethylcinnamate, gave only 18% yield. All in all, it appears that the reaction conditions developed above are quite specialized for the substrates with which they were developed. The poor yields for the other substrates also demonstrate the poor catalytic ability of the iridium in relation to rhodium, which gives excellent yields with the majority of the substrates tested in this study (with the *m*-nitrophenyl and the olefinic boronic acid being the sole exceptions).

The most important information to come out of this research, is the fact that iridium has been shown for the first time to be a catalyst for 1,4 conjugate addition reactions. To date there have been no other reports of iridium complexes being used in this fashion. However, the poor reactivity of the iridium hydroquinone catalyst may mean that further development in this area of catalysis will be limited. Even though the iridium system may be far cheaper than rhodium, the inability of the iridium benzoquinone to react with abroad range of substrates gives the catalyst system a limited appeal. While it may be possible under some conditions to obtain high yields for 1,4 conjugate addition reactions catalyzed by iridium, in all likelihood these conditions will not be as efficient as those with rhodium, thus negating any cost benefit that might be gained by choosing former.

3. Experimental

All reactions were carried out under N_2 in flame-dried glassware. $[Ir(COD)Cl]_2$ was purchased from Strem Chemical Co. The ^1H NMR spectra were recorded by Bruker (300 MHz) spectrometer. Elemental analyses were performed by Quantitative Technologies Inc.

Table 4
Iridium catalyzed 1,4 conjugate addition reactions with various boronic acids.



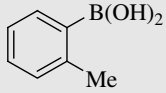
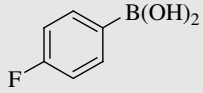
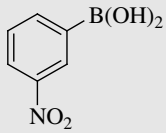
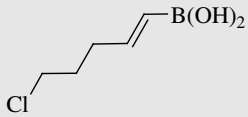
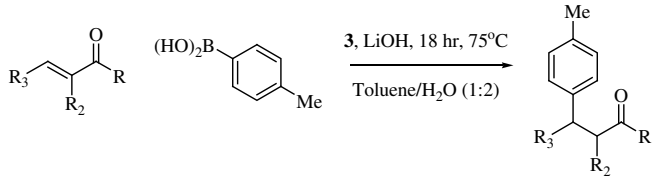
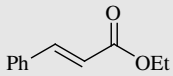
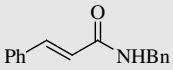
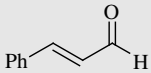
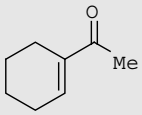
Entry	Boronic acid	% Yield	Entry	Boronic acid	% Yield
1		57	3		18
2		0	4		0

Table 5
Iridium catalyzed 1,4 conjugate addition reactions with various electron deficient olefins.



Entry	Substrate	% Yield	Entry	Substrate	% Yield
1		14	3		0
2		0	4		0

3.1. Synthesis of $^{+}BF_4^{-}$)(η^6-hydroquinone)Ir(COD)$^{+}BF_4^{-}$ (**3**$^{+}BF_4^{-}$)

[Ir(COD)Cl]$_2$ (0.20 g, 0.30 mmol) and $AgBF_4$ (0.14 g, 0.71 mmol) were dissolved in methylene chloride (5 mL) and acetone (1 ml), respectively, and combined in a flame-dried one neck schlenk tube. While stirring, a white precipitate of AgCl formed on the bottom of the glassware. After 1 h, 1,4-hydroquinone (0.13 g, 1.2 mmol), dissolved in 2 mL of acetone, was added to the reaction mixture. After stirring for 4 h at room temperature, the solvent was removed via a rotary evaporator. The residue was dissolved in methylene chloride (3 mL) and then filtered slowly (dropwise) through a celite plug into 100 mL of diethyl ether. The resulting white precipitate was filtered and washed three times with 10 mL aliquots of diethyl ether. The product was recrystallized from methylene chloride by cooling a solution in a freezer at −30 °C. The recrystallized product was filtered through a fritted glass filter and dried under vacuum. The isolated yield was 88% (0.25 g, 0.52 mmol). ^{1}H NMR (CD_2Cl_2): δ 8.40 (br.s, 2H), δ 6.27 (s, hydroquinone ring, 4H), δ *4.37 (br.s,* olefinic COD protons, 4H), δ *2.25 (m,* aliphatic COD protons, 4H), δ 2.12 (m, aliphatic COD protons, 4H).). ^{1}H NMR (CD_3OD): δ 6.25 (s, 4H), δ 4.30 (m, 4H), δ 2.25(m, 4H), δ 2.19 (m, 4H). Elemental Anal. Calc.: C, 33.81; H, 3.65. Found: C, 33.78; H, 3.35%.

3.2. Deprotonation of $^{+}BF_4^{-}$)(η^6-hydroquinone)Ir(COD)$^{+}BF_4^{-}$ (**3**$^{+}BF_4^{-}$)

A solution of **3**$^{+}BF_4^{-}$ in D_2O was rapidly deprotonated by LiOH to afford a stable solution of (η^4-quinone)Ir(COD)$^{-}$. ^{1}H NMR (D_2O): δ 6.25 (s, 4H), δ 4.38 (m, 4H), δ 2.32(m, 4H), δ 2.24 (m, 4H) after the addition of LiOH changed to. δ 5.38 (s, 4H), δ 3.85 (m, 4H), δ *2.16 (m,* 4H), δ 2.04 (m, 4H). These changes are analogous to those seen with the rhodium analogues, which have been fully characterized [1,2].

3.3. Typical catalytic procedure

A 1 dram vial fitted with a Teflon cap was charged with *p*-tolylboronic acid (205 mg, 1.5 mmol, 3 equiv.), 2-cyclohexen-1-one (48 mg, 0.5 mmol, 1.0 equiv.), and toluene (1.0 mL). To this mixture was added the iridium catalyst **3** (7.5 mg, 0.015 mmol, 3 mol%) followed by an aqueous LiOH solution (1.0 M, 0.090 mL, 0.090 mmol, 18 mol%). The headspace of the vial was filled with 2 mL of deoxygenated H_2O and was flushed with nitrogen and sealed. The resulting mixture was stirred at 75 °C for 18 h. Following this period of time the reaction mixture was diluted in 4 ml of a 1:1 mixture of ethyl acetate and hexanes, and washed sequentially with saturated solution of NH_4Cl (5 mL), 1 N NaOH and brine. The organic layers were combined, dried over sodium sulfate, filtered through a silica plug, and concentrated under reduced pressure to afford pure product as a clear oil in 60% yield (56 mg).

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Appendix A. Supplementary material

NMR of the products of the catalytic reactions. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2008.09.066.

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