# **ORGANOMETALLICS**

# Disambiguation of Metal and Brønsted Acid Catalyzed Pathways for Hydroarylation with Platinum(II) Catalysts

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#### Supporting Information

**ABSTRACT:** The hydroarylation of unactivated olefins effected by Pt(II) precatalysts was found to proceed through the in situ production of protic acid followed by a Friedel—Crafts mechanism. The reaction was investigated using the hindered base 2,6-di-*tert*-butyl-4-methylpyridine and a variety of substrates.



The hydroarylation of alkenes may be defined as the addition of an arene C-H bond across the C=C bond of an alkene to produce an alkyl arene (eq 1). Homogeneous transition-metal complexes, especially those of Pt(II), are potentially useful catalysts for alkene hydroarylation, because they can produce uniquely controlled distributions of isomers as products. In principle, the product distributions can be manipulated further through ligand tuning.<sup>1-5</sup> At the same time, these catalysts could eliminate the current need for costly, toxic, and wasteful activated substrates such as halogenated compounds for the preparation of substituted aromatics.<sup>6-9</sup>

$$R \longrightarrow + \square \xrightarrow{Pt(II) \text{ catalyst}} R \xrightarrow{Pt(II) \text{ or } R} (1)$$

Recently, mechanistic investigations by Gunnoe and co-workers of (4,4'-<sup>t</sup>Bu<sub>2</sub>bipy)PtPh<sup>+</sup> as a hydroarylation catalyst revealed that activation of the arene C—H bond at the metal center was a key step.<sup>5</sup> Goldberg and co-workers uncovered similar mechanistic findings with a related system. They found that, in the coupling of propene with toluene catalyzed by (3,5-dimethyl-2-(2-pyridyl)pyrrolide)PtPh(SMe<sub>2</sub>), meta-substituted products were favored, and both Markovnikov and anti-Markovnikov products were observed in a 6:1 ratio.<sup>2</sup>

Herein, we describe a study of the mechanism of alkene– arene coupling by  $Pt(COD)(OTf)_2$  (1a) and  $Pt({}^tBu_2bipy)$ - $(OTf)_2$  (1b) (COD = 1,5-cyclooctadiene;  ${}^tBu_2bipy$  = 4,4'-di*tert*-butyl-2,2'-bipyridine; OTf = trifluoromethanesulfonate). The coupling of norbornene and benzene to form *exo*-phenylnorbornane (2a) has been reported using catalyst 1a.<sup>3</sup> Complex 1a was chosen for further study because it appeared likely to act through a mechanism distinct from the known arene C–H activation pathway. One piece of evidence for a distinct mechanism was that the related catalyst  $[(\eta^2-C_2H_4)PtCl_2]_2$  with AgBF<sub>4</sub> in *o*-dichlorobenzene gave strong ortho/para selectivity for the coupling of norbornene and toluene.<sup>3</sup> In addition, it was found that 1a activated alkenes such as norbornene to generate vinylic C–H insertion products and release triflic acid.<sup>10</sup> The studies presented here give evidence for an alkene–arene coupling mechanism in which the active catalyst is an acid that has been produced via an alkene coupling reaction facilitated by 1.

Our initial experiments focused on optimization of reaction conditions for the coupling of norbornene and benzene. The highest yield was achieved with a 9-fold excess of benzene compared to norbornene at 110  $^{\circ}$ C, which produced **2a** in 41% yield after 5 h (eq 2).

9 + 
$$2a$$
 (COD)Pt(OTf)<sub>2</sub>, 10 mol%  
 $-C_6H_4Cl_2$  (2)  
 $110 \,^\circ\text{C}, 5 \,\text{h}$   $2a$ 

Since the norbornene substrate was consumed in the hydroarylation reactions, but yields of **2a** were still low, it was of interest to identify competing side reactions. <sup>1</sup>H NMR spectroscopic studies revealed that the reaction of norbornene to form the isomer nortricyclene (**3**) is efficient under the reaction conditions, slowing down the desired coupling reaction (eq **3**). The competitive isomerization of norbornene, despite its reaction-favoring strain

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energy and its common use in related experiments,<sup>3</sup> prompted investigation of other alkenes for the coupling reaction.

$$(COD)Pt(OTf)_2, 10 mol\%$$

$$2:1 o - C_6 H_4 Cl_2: C_6 H_6$$

$$25 °C$$

$$3$$

$$(3)$$

Cyclic alkenes are appealing substrates, since isomerization of these alkenes does not affect the efficiency or selectivity of product formation. When cyclohexene was heated to  $100 \,^{\circ}$ C for 24 h in the presence of 9 equiv of benzene and 10 mol % 1a, cyclohexylbenzene (2b) was produced in moderate yield (36%), but dicyclohexylbenzene (2c) was also generated in 21% yield as a mixture of isomers (eq 4).



The formation of **2c** suggested that more electron-rich arenes such as **2b** might be more susceptible to the coupling reaction than benzene. Indeed, the electron-poor arene *o*-dichlorobenzene did not undergo observable hydroarylation, and the relative reactivity of four different arenes was found to increase with their nucleophilicity: *o*-dichlorobenzene < chlorobenzene < benzene < mesitylene.

The catalytic coupling reaction of cyclohexene and mesitylene with 10 mol % 1a gave a quantitative yield of 1-cyclohexyl-2,4,6-trimethylbenzene (2d) after 4 h at 100 °C, and no multiply coupled products were observed (eq 5a). This result provided a suitable subject for mechanistic investigations; therefore, experiments were undertaken to determine whether the reaction mechanism for this process included C–H activation<sup>2,5</sup> or Friedel–Crafts pathways.<sup>11–14</sup>



Experiments were carried out to determine the role of protons in the observed catalysis. The hydroarylation reaction shown in eq 5 was run with 20 mol % triflic acid in place of 1a as the catalyst (eq 5b). Triflic acid was observed to be a good catalyst for the coupling reaction: a quantitative yield of 2d was obtained in less than 1 h at 100 °C. This result confirmed that a Brønsted acid can catalyze the effective hydroarylation of cyclohexene by mesitylene.

To determine whether such a triflic acid catalyzed mechanism was responsible for the coupling observed with 1a as a catalyst precursor, the catalytic reaction was run in the presence of the noncoordinating base 2,6-di-*tert*-butyl-4-methylpyridine (eq 6).



Base (1 or 2 equiv with respect to 1a) was added to a solution of cyclohexene and 10 mol % 1a in mesitylene (9 equiv with

respect to cyclohexene) and *o*-dichlorobenzene. In each case, the conjugate acid of the pyridine was observed by <sup>1</sup>H NMR spectroscopy as resonances at 10.7-10.9 ppm for the N-H proton.<sup>17</sup> In the presence of 1 equiv of added base only 29% of the product **2d** was produced, and with 2 equiv of base, only 2% of **2d** was generated. These results establish that under the coupling conditions, a protic acid was available in solution, and this acid was essential to product formation.

Manipulation of the experimental conditions in the presence of the base additive demonstrated that the combination of cyclohexene and the platinum precursor was the source of the protic acid. Pyridinium ion was not observed under the reaction conditions in the absence of cyclohexene, even at extended reaction times (18 h). When the reaction was run using perdeuterated benzene in place of the mesitylene/*o*-dichlorobenzene solvent mixture, with 10 mol % of **1a** and 1 equiv of cyclohexene, the protonated base was observed after 18 h at 100 °C. These results strongly suggest that the source of the protons in the reaction mixture is cyclohexene. Pt-mediated coupling of cyclohexene could generate 1 equiv of HOTf, as shown by Szuromi and Sharp (eq 7).<sup>10</sup>

2 
$$\longrightarrow$$
 + Pt(COD)(OTf)<sub>2</sub>  $\longrightarrow$   $Pt(COD)$   $OTf^{\bigcirc}$  + HOTf (7)

The observation of olefin dimers as side products during the catalytic runs provided additional evidence for the generation of HOTf via alkene coupling. For example, when a solution of norbornene, 9 equiv of benzene, and 10 mol % **1a** in *o*-dichlorobenzene was heated for 5 h (eq 2), a side product was observed by GC-MS ( $M^+$  at m/z 188) with a mass equivalent to  $C_{14}H_{20}$ , a norbornene dimer. Such a dimer is consistent with Pt-mediated production of HOTf.<sup>10</sup>

To eliminate the possibility that coupling of the COD ligand at Pt is the major source of protons, the related catalyst **1b** was studied. Complex **1b** exhibited hydroarylation reactivity nearly identical with that of complex **1a**, and the reaction was also inhibited by the addition of base.

To show that the catalyst was a soluble species, rather than heterogeneous Pt(0), the optimized reaction shown in eq 5a was run in the presence of Hg(0) with vigorous stirring. The catalysis was not inhibited.<sup>15,16</sup>

As a final test for a mechanism that requires proton release by cyclohexene coupling, 1,2-diphenylacetylene (4) was used as a hydroarylation substrate.

Substrate 4 does not possess vinylic protons and therefore is unable to produce HOTf by the proposed coupling mechanism. Treatment of substrate 4 with 10 mol % of **1b** and 6 equiv of mesitylene in *o*-dichlorobenzene for 4 h at 100 °C gave hydroarylation products in only 14% yield (Table 1, entry 1). The presence of a small amount of hydroarylation products can be explained by the Pt species acting as a Lewis acid. For comparison, the simple Lewis acid AgOTf, at 20 mol % catalyst loading, gave 37% yield of product **2d** under the same conditions. In contrast to the low-yielding Pt-catalyzed reaction, hydroarylation products were observed in quantitative yield after 4 h at 100 °C (Table 1, entry 2) when HOTf was used in place of **1b** as the catalyst. In order to elucidate the role of cyclohexene, the hydroarylation of **4** with **1b** as catalyst was carried out in the presence of 20 mol % cyclohexene as a cocatalyst, and the yield

# Table 1. Hydroarylation of 1,2-Diphenylacetylene (4)



entry	tal.	yield of flydroarylation products (70)
1	1b	14
2	HOTf	>95
3	1b + cyclohexene, 20%	65

# Scheme 1. Mechanism of Hydroarylation



increased to 65% (Table 1, entry 3). These three outcomes support a mechanism in which cyclohexene undergoes reaction at the Pt center to produce a small amount of HOTf, which then serves as a hydroarylation catalyst by the Friedel–Crafts mechanism (Scheme 1).<sup>11–14</sup>

The Friedel—Crafts mechanism is consistent with recent work showing that several other transition-metal catalyzed reactions also operate through production of a small amount of a Brønsted acid, which then becomes the active catalyst for the transformation.<sup>18,19</sup>

In summary, complexes 1a,b were found to catalyze the coupling of alkenes with arenes, and the best results were obtained for cyclohexene and mesitylene. Evidence from studies with added base, with an acid catalyst, and with an alternative substrate has been presented to support the mechanism illustrated in Scheme 1. Small concentrations of acid are produced by an interaction between Pt and the alkene, and the liberated HOTf acts as a catalyst for a Friedel-Crafts alkylation mechanism. This work, by suggesting a surprisingly simple mechanism, raises questions about the precise role of protons and metals in other catalytic alkene-arene coupling reactions, where acid may also be produced, and proton catalyzed pathways may be responsible for decreasing selectivities. We recommend that thorough control experiments for acid catalysis become standard protocol for all new reactions of organometallic catalysts, even when no acid is present in the starting materials.

# ASSOCIATED CONTENT

**Supporting Information**. Text, tables, and figures giving experimental details for catalytic runs and control reactions. This material is available free of charge via the Internet at http://pubs. acs.org.

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