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Iridium-Catalyzed Hydroarylation of Conjugated Dienes *via* π -Allyliridium Intermediates

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Supporting Information Placeholder

ABSTRACT: A hydroxoiridium/cod complex efficiently catalyzed hydroarylation of conjugated dienes with arenes bearing an acidic N–H bond as a directing group, which can form an amidoiridium species as an active intermediate for C–H activation. A π -allyliridium(III) complex was isolated as a key intermediate leading to the addition product.

Direct functionalization of aromatic rings under transition-metal catalysis has steadily expanded the range of choices for organic transformations.¹ In particular, catalytic hydroarylation,^{1–3} which involves addition of aromatic C–H bonds to unsaturated compounds, is one of the most atom- and step-economical reactions in the aromatic alkylation. In this respect, conjugated dienes are useful reaction partners in the hydroarylation, leading to alkenyl arenes.^{4–6} For example, Nakao and Hiyama reported Ni-catalyzed hydroarylation of 1-phenyl-1,3-butadiene with pentafluorobenzene, where the addition occurs at the terminal double bond to give a branched adduct.^{4a} It is proposed that the reaction proceeds *via* a π -allylnickel intermediate. Ong reported Ni-catalyzed switchable hydroheteroarylation of cyclic dienes.^{4b} Conjugated dienes are also subject to electrophilic activation by π -acidic metal complexes, which enables alkylation of electron-rich aromatic compounds.⁵

We recently reported that hydroxoiridium complexes efficiently catalyze branch-selective hydroarylation of vinyl ethers with *N*-sulfonylbenzamides bearing an acidic N–H bond, where deprotonation of the amide with the hydroxoiridium gives an amidoiridium(I) species as a key intermediate for C–H activation forming a hydridoiridium(III) species (Scheme 1).⁷ It is proposed that migratory insertion of vinyl ethers into the Ir–C bond followed by reductive elimination gives the branched adduct. Here we report that conjugated dienes are good substrates in the iridium-catalyzed hydroarylation with

benzamides giving the addition products with high regioselectivity. Mechanistic studies indicated that the reaction proceeds *via* a π -allyliridium(III) intermediate, and subsequent reductive elimination leading to the addition product was found to

Scheme 1. Hydroxoiridium-Catalyzed Hydroarylation

be promoted by *N*-sulfonylbenzamides.

Treatment of 3-methyl-*N*-(methanesulfonyl)benzamide (**1a**) with 1.2 equiv of 1-phenyl-1,3-butadiene (**2a**) in the presence of [Ir(OH)(cod)]₂ (5 mol % of Ir, cod = 1,5-cyclooctadiene) in toluene at 70 °C for 12 h gave the branched adduct **3aa** in 95% yield as a single regioisomer (Scheme 2). Amide **1b** bearing *p*-toluenesulfonyl group displayed as high reactivity as **1a**, whereas the reaction of primary amide **1c** did not give the adduct. These results indicate that the high acidity of the N–H

proton is essential for the formation of the amidoiridium species *via* deprotonation by the hydroxoiridium. The reaction was completely inhibited by the presence of binap as a ligand. The rhodium complex [Rh(OH)(cod)]₂ displayed no catalytic activity (see the Supporting Information).

The results obtained for the hydroarylation of diene **2a** with

Scheme 2. Hydroarylation of **2a** with Benzamides **1a**

^a Reaction conditions: **1** (0.20 mmol), **2a** (0.24 mmol), and [Ir(OH)(cod)]₂ (5 mol % Ir) in toluene (0.80 mL) at 70 °C for 12 h. Isolated yields are shown.

Scheme 3. Hydroarylation of **2a** with Arenes **1a**

^a Reaction conditions: **1** (0.20 mmol), **2a** (0.24 mmol), and [Ir(OH)(cod)]₂ (5 mol % Ir) in toluene (0.80 mL) at 70 °C for 12 h. Isolated yields are shown. ^b Isolated yield after *N*-methylation. ^c In ClCH₂CH₂Cl. ^d [Ir(OH)(cod)]₂ (10 mol % Ir).

various arenes **1** are summarized in Scheme 3. The reaction of several benzamides **1d–h** bearing *meta*- and *ortho*-substituents gave the corresponding adducts **3da–ha** in 83–95% yields. Naphthyl rings and a heteroaromatic ring also participated in the reaction to give the adducts **3ia–ka** in good yields. Not only *N*-sulfonylamides but also some other nitrogen-based functional groups bearing acidic N–H bonds were capable of the hydroarylation: 2-aryl-4-quinazolinone⁸ **1l** and **1m** underwent the alkylation to give **3la** and **3ma**, respectively, in good yields. The reaction of 3-arylbenzothiadiazine-1,1-dioxide **1n** gave **3na** in 95% yield. 2-Arylindole **1o**^{7c} also reacted with **2a** to give **3oa** in moderate yield.

As shown in Scheme 4, a variety of conjugated dienes participated in the reaction to give the corresponding hydroarylation products. The reactions of 1-aryl-1,3-butadienes **2b–d** gave **3ab–ad** in high yields. Interestingly, hydroarylation of

Scheme 4. Hydroarylation of **2** with Benzamide **1a**

^a Reaction conditions: **1a** (0.20 mmol), **2** (0.24 mmol), and [Ir(OH)(cod)]₂ (5 mol % Ir) in toluene (0.80 mL) at 70 °C for 12 h. Isolated yields are shown. ^b In ClCH₂CH₂Cl. ^c Contains isomers (see Supporting Information for details). ^d **2f** (5.0 equiv) for 24 h. ^e At 80 °C for 24 h. ^f **2j** (3.0 equiv) at 80 °C for 24 h. ^g For 24 h.

(*Z*)-**2d** gave (*E*)-**3ad** exclusively in 82% yield along with the recovery of **2d** as a mixture of *E* and *Z* isomers.⁹ Hydroarylation of aliphatic dienes **2e** and **2f** gave **3ae** and **3af**, respectively, in high yields together with a small amount of their isomers.¹⁰ Diene **2g** bearing a cyclic alkene moiety also reacted to give **3ag** in moderate yield, where hydroarylation occurred at the vinyl group. The reaction of an internal diene **2h** proceeded with high regioselectivity to give **3ah**, albeit in low yield. Dienoate **2i** also participated in the reaction to give δ -lactam **4ai** generated by intramolecular cyclization of the initial hydroarylation product.¹¹ It should be noted that electron-withdrawing substituents on dienes significantly improved their reactivity: internal dienes **2j–l** bearing carbonyl groups gave **4aj–al** in good yields with high diastereoselectivity. Unfortunately, 2,3- nor 1,3-disubstituted diene (**2m** nor **2n**) was reactive in the present reaction.

When the progress of the reaction of **1a** with **2a** was monitored by ¹H NMR, the formation of a new species **5aa** was observed, and the amount of the species remained constant from the beginning of the reaction (Figure 1). The species **5aa** was tentatively assigned to be a π -allyliridium complex¹² by NMR and HRMS after isolation from other reactants. The ¹H NMR chemical shifts of the allyl group in **5aa** are 6.67 ppm (d, *J* = 12.9 Hz), 4.19 ppm (dd, *J* = 12.9, 9.6 Hz), and 3.65 ppm (dq, *J* = 9.6, 6.8 Hz) in CDCl₃. Iridium complex **5aa** was stable for more than 48 h at room temperature in CDCl₃ and at least for 6 h even at 50 °C in benzene-*d*₆.

There are two possible reaction pathways for the present hydroarylation (Scheme 5): one involves insertion of an alkene moiety of **2** into an Ir–H of an aryl(hydrido)iridium(III) species (hydroiridation) to form π -allyliridium **5** followed by re-

Figure 1. Observation of allyliridium **5aa**: plot of the conversion and yields vs. time.

ductive elimination of the C–C bond (*Path a*). The other pathway consists of alkene insertion into an Ir–C bond (carboiridation) and reductive elimination of the C–H bond (*Path b*). In the previous reports on iridium-catalyzed hydroarylation of alkenes, experimental and theoretical studies indicated that carboiridation is the productive pathway while reversible hydroiridation occurs.^{7b,13} The reactivity of **5aa** was further examined to find out whether it is an intermediate or a resting state. As shown in Scheme 6a, **5aa** did not undergo either C–C bond formation or allyl ligand exchange in the presence of diene **2i**. In contrast, treatment of **5aa** with *N*-tosylamide **1b**

Scheme 5. Possible Reaction Pathways

Scheme 6. Intermediacy of Allyliridium 5aa

a) Reaction of **5aa** with 1,3-diene **2i**

b) Reaction of **5aa** with amide **1b**

led to the exclusive formation of adduct **3aa** (Scheme 6b). The absence of the crossover products such as **5ba** and **3ba** implies that π -allyl complex **5aa** directly gives **3aa** without dissociation of diene **2a** from **5aa** by β -hydride elimination. The presence of *N*-mesylamide **1a** also promoted the conversion of **5aa** into **3aa**, and increasing the amount of **1a** accelerated the formation of **3aa** (see Figure S2). It is likely that amide **1b** having the acidic N–H group promotes the reductive elimination forming **3aa** by protonation of the amide moiety in **5aa**, as the addition of acetic acid, which is not a competent substrate, also gave **3aa** (see Scheme S2).¹⁴

The catalytic cycle is postulated as illustrated in Scheme 7. A hydroxoiridium complex reacts with amide **1** to form amidoiridium(I) species **A**. Oxidative addition of *ortho*-C–H bond to the iridium gives hydridoiridium(III) intermediate **B**, which reacts with diene **2** to generate π -allyliridium(III) species **C**. Reductive elimination from allyliridium **C** in the presence of amide **1** gives the corresponding hydroarylation product **3** and regenerates amidoiridium species **A**. A deuterium-labeling experiment suggests that oxidative addition and insertion of dienes forming alkyliridium **D** are fast and reversible (see Scheme S4).¹⁵ The turnover-limiting step might be reductive elimination, although it should be noted that insertion of internal dienes into Ir–H is significantly slower than that of terminal dienes (see Figure S3).

In conclusion, we have developed the hydroxoiridium-catalyzed hydroarylation of conjugated dienes *via* C–H activation. The reactions of various dienes with arenes bearing an

Scheme 7. Plausible Catalytic Cycle

acidic N–H bond proceeded to give the corresponding adducts with high regioselectivity. Mechanistic studies were in good agreement with the proposed catalytic cycle involving the π -allyliridium(III) intermediate, where reductive elimination of the species was promoted by *N*-sulfonylbenzamides as substrates.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental procedures and compound characterization (PDF)

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Notes

The authors declare no competing financial interest.

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(9) The exclusive formation of (*E*)-**3ad** can be explained by *syn/anti* isomerization of the allyliridium. The recovery of (*E*)-**2d** is not necessarily due to dissociation of **2d** from allyliridium **5ad** because *E/Z* isomerization of **2d** proceeded even in the absence of **1a**. See Scheme S3.

(10) The regioisomers are likely to be formed via hydroarylation of internal dienes resulting from double bond isomerization of **2e** and **2f**. Hydrogenation of **3ae** and **3af** gave the corresponding saturated compounds as a mixture of isomers. See the Supporting Information.

(11) The crude mixture contains both hydroarylation product **3** and cyclization product **4**. The hydroarylation product was completely converted into the cyclization product through the isolation by preparative TLC on silica gel.

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