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<th>Citation</th>
<th>Organic Letters, 20(3): 828-831</th>
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<td>Issue Date</td>
<td>2018-01-11</td>
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<tr>
<td>Type</td>
<td>Journal Article</td>
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<td>Textversion</td>
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<td>Supporting Information</td>
<td>The Supporting Information is available free of charge on the ACS Publications website at <a href="https://doi.org/10.1021/acs.orglett.7b03969">https://doi.org/10.1021/acs.orglett.7b03969</a>.</td>
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<tr>
<td>DOI</td>
<td>10.1021/acs.orglett.7b03969</td>
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Iridium-Catalyzed Hydroarylation of Conjugated Dienes via $\pi$-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 $\pi$-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. In particular, catalytic hydroarylation, 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. 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. It is proposed that the reaction proceeds via a $\pi$-allylnickel intermediate. Ong reported Ni-catalyzed switchable hydroheteroarylation of cyclic dienes. Conjugated dienes are also subject to electrophilic activation by $\pi$-acidic metal complexes, which enables alkylation of electron-rich aromatic compounds.

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). 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 $\pi$-allyliridium(III) intermediate, and subsequent reductive elimination leading to the addition product was found to 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)]; (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 regiosomer (Scheme 2). Amide 1b bearing p-toluene sulfonyl 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 \([\text{Rh(OH)(cod)}]_2\) displayed no catalytic activity (see the Supporting Information).

The results obtained for the hydroarylation of diene 2a with various arennes 1 are summarized in Scheme 3. The reaction of several benzamides 1d–h bearing meta- and ortho-substituents gave the corresponding adducts 3a–h 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-quinoxalinone 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 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 2. Hydroarylation of 2a with Benzamides 1**

![Diagram](image)

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

![Diagram](image)

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

![Diagram](image)
(Z)-2d gave (E)-3ad exclusively in 82% yield along with the recovery of 2d as a mixture of E and Z isomers. Hydroarylation of aliphatic dienes 2e and 2f gave 3ae and 3af, respectively, in high yields together with a small amount of their isomers. 2g Diene bearing a cyclic alkene moieties 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. 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 complex 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-d6.

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 reductive elimination of the C–H bond to the iridium gives hydridoiridium(III) intermediate A hydroxoiridium 5a and reductive elimination forming 3aa having the acidic N–H group promotes the concomitant reduction of the amide moiety in 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).

The catalytic cycle is postulated as illustrated in Scheme 7. A hydroxoiridium complex reacts with amide 1 to form amidoiridium(1) species A. Oxidative addition of ortho-aryl–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 deuteration-labeling experiment suggests that oxidative addition and insertion of dienes forming allyliridium D are fast and reversible (see Scheme S4). 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
acetic 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.

ACKNOWLEDGMENT

This work was supported by JSPS KAKENHI Grant Number JP15H03810. M.N. thanks to the JSPS for Research Fellowship for Young Scientists.

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(8) 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.

6b) 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.