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**COMMUNICATION****Ruthenium-catalyzed alkenylation of azoxybenzenes with alkenes through *ortho*-selective C–H activation**Hongji Li,<sup>a</sup> Xiaoyu Xie,<sup>a</sup> and Lei Wang<sup>\*a,b</sup>

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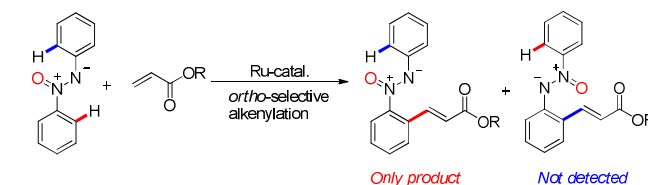
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A highly selective alkenylation of azoxybenzenes catalyzed by Ru<sup>III</sup>-complex was developed. It provides a direct access to a series of olefinated azoxy compounds in good yields.

Recently, transition metal-catalyzed alkenylation of C–H bonds has been one of most practical, atom- and step-economical method in synthetic organic chemistry.<sup>1</sup> Especially noteworthy is that Fujiwara's group has made the initial work on the catalytic alkenylation of electron-rich aromatic C–H bond with alkenes by palladium complex.<sup>2</sup> After that, palladium catalyst was broadly employed in the catalytic alkenylation of functionalized substrates.<sup>3</sup> In addition, rhodium-catalyzed alkenylations of amides, esters and ketones were also developed in recent years.<sup>4</sup> Most recently, ruthenium complexes have been exploited as alternative catalysts for the direct C–H bond alkenylations.<sup>5</sup> For example, Ackerman,<sup>5a,b</sup> Wang,<sup>5c,d</sup> and others<sup>5e-h</sup> have done the excellent work on the Ru-catalyzed alkenylations. However, more substrates containing new tolerated directing groups and occurring regio-selective at their *ortho*-positions were necessary to be explored. As far as we know, the useful azoxybenzenes with two kinds of C–H bonds at the *ortho*-position of the nitrogen atom has been rarely studied in group-directed C–H activation and functionalizations.<sup>6</sup>

Azoxo compounds are important materials and useful intermediates in electronic devices for their liquid crystalline properties,<sup>7</sup> and they have also been used as dyes, polymer inhibitors and stabilizers.<sup>8</sup> In light of their importance, numerous methods for the preparation of azoxy compounds have been developed.<sup>9</sup> However, there is no report on the synthesis of *ortho*-alkenyl azoxybenzenes. Very recently, Ru<sup>II</sup>-catalyzed C–H bond activation and functionalizations have been reported,<sup>5,10</sup> and which promoted us to explore the possibility of Ru<sup>III</sup>-catalyzed alkenylation of azoxybenzenes with alkenes. As part of our ongoing interest in C–H activation,<sup>11</sup> herein we wish to report the first Ru<sup>III</sup>-catalyzed *ortho*-selective alkenylation of azoxybenzenes, which provided a simple approach to a variety of olefinated azoxy compounds (Scheme 1).

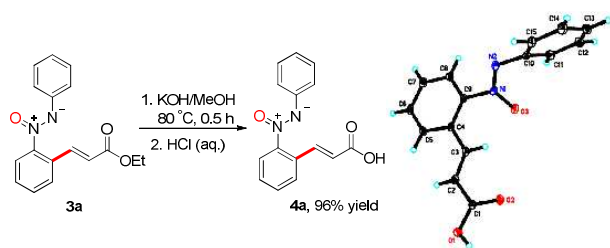
The initial reaction of azoxybenzene (**1a**) with ethyl acrylate (**2a**) was carried out in the presence of 2.5 mol % of [ $\text{RuCl}_2(p\text{-cymene})_2$ ] and  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (1.0 equiv) in 1,2-dichloroethane (DCE) at 110 °C for 12 h, which only generated the mono-substituted alkenylation product **3a** in 17% yield (Table 1, entry 1). The structure of **3a** was indirectly confirmed by the hydrolysis of **3a** into its carboxylic acid **4a** in  $\text{NaOH}/\text{CH}_3\text{OH}$ ,<sup>12</sup> and the structure of **4a** was further determined by X-ray single crystal analysis, as described in Scheme 2 (details in Supporting Information). After that, the use of anhydrous  $\text{Cu}(\text{OAc})_2$  was investigated in the model reaction under nitrogen atmosphere,

Scheme 1. Ru<sup>III</sup>-catalyzed *ortho*-selective alkenylationTable 1. Optimization of Ru source and additives<sup>a</sup>

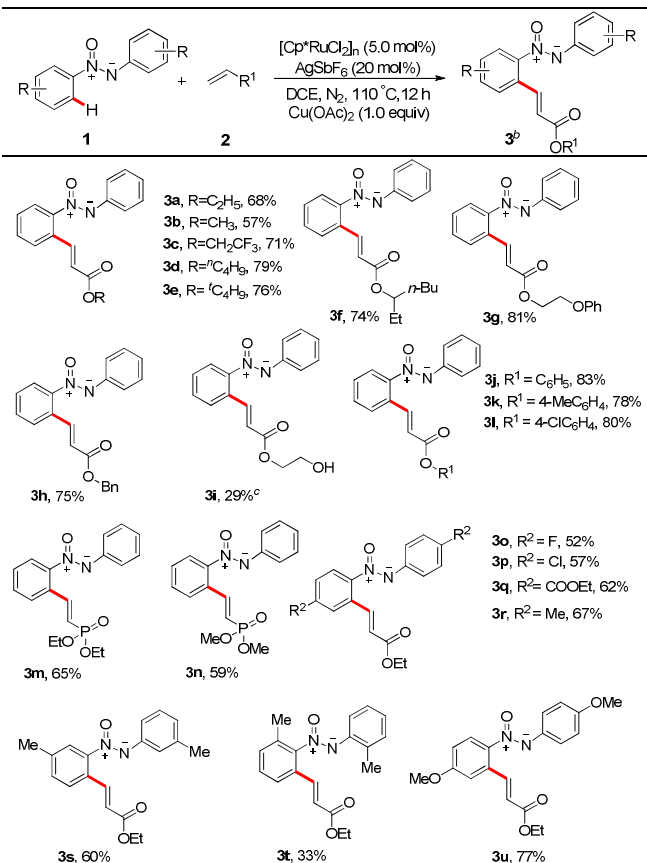
Entry	Ru source	Additive 1 (1.0 equiv)	Additive 2 (mol%)	Yield (%) <sup>b</sup>
1	[RuCl <sub>2</sub> L] <sub>2</sub>	Cu(OAc) <sub>2</sub> · H <sub>2</sub> O	/	17
2	[RuCl <sub>2</sub> L] <sub>2</sub>	Cu(OAc) <sub>2</sub>	/	29
3	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	Cu(OAc) <sub>2</sub>	/	35
4	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	Cu(OAc) <sub>2</sub>	KPF <sub>6</sub> (10)	33
5	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	Cu(OAc) <sub>2</sub>	AgSbF <sub>6</sub> (10)	56
6	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	Cu(OAc) <sub>2</sub>	AgSbF <sub>6</sub> (20)	68
7	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	Cu(OAc) <sub>2</sub>	AgSbF <sub>6</sub> (30)	70 <sup>c</sup>
8	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	Cu(OAc) <sub>2</sub>	AgSbF <sub>6</sub> (20)	62 <sup>d</sup>
9	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	Cu(OAc) <sub>2</sub>	AgSbF <sub>6</sub> (20)	69 <sup>e</sup>
10	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	Cu(OAc) <sub>2</sub>	AgSbF <sub>6</sub> (20)	51 <sup>f</sup>
11	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	Cu(OAc) <sub>2</sub>	AgSbF <sub>6</sub> (20)	70 <sup>g</sup>
12	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	Cu(OAc) <sub>2</sub>	AgSbF <sub>6</sub> (20)	41 <sup>h</sup>
13	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	AgOAc	AgSbF <sub>6</sub> (20)	24
14	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	Ag <sub>2</sub> CO <sub>3</sub>	AgSbF <sub>6</sub> (20)	11
15	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	/	AgSbF <sub>6</sub> (20)	0
16	[Cp*RuCl <sub>2</sub> ] <sub>n</sub>	/	AgSbF <sub>6</sub> (20)	0 <sup>i</sup>

<sup>a</sup> Reaction conditions: azoxybenzene (**1a**, 0.20 mmol), ethyl acrylate (**2a**, 0.30 mmol), Ru complex (containing 5.0 mol% Ru), additive **1** (0.20 mmol), additive **2** amount indicated in this Table in DCE (1.0 mL) at 110 °C under N<sub>2</sub> for 12 h. <sup>b</sup> Isolated yields. <sup>c</sup> 30 mol % of AgSbF<sub>6</sub>. <sup>d</sup> 90 °C. <sup>e</sup> 130 °C. <sup>f</sup> 8 h. <sup>g</sup> 15 h. <sup>h</sup> Molar ratio of **1a** with **2a** = 1:2. <sup>i</sup> **2a** (0.60 mmol) was used. Cp\* = pentamethylcyclopentadienyl, L = *p*-cymene.

and 29% of **3a** was isolated (Table 1, entry 2). To our delight, enhanced yield of **3a** was observed in the presence 5.0 mol% of [Cp\*RuCl<sub>2</sub>]<sub>n</sub> as catalyst (Table 1, entry 3). Some other common additives, such as KPF<sub>6</sub> and AgSbF<sub>6</sub>, were also examined and result showed that the employment of AgSbF<sub>6</sub> (20 mol%) obviously accelerated this transformation (Table 1, entries 4–7).



**Scheme 2.** Hydrolysis of **3a** into **4a**, and the structure of **4a** determined by X-ray single crystal analysis

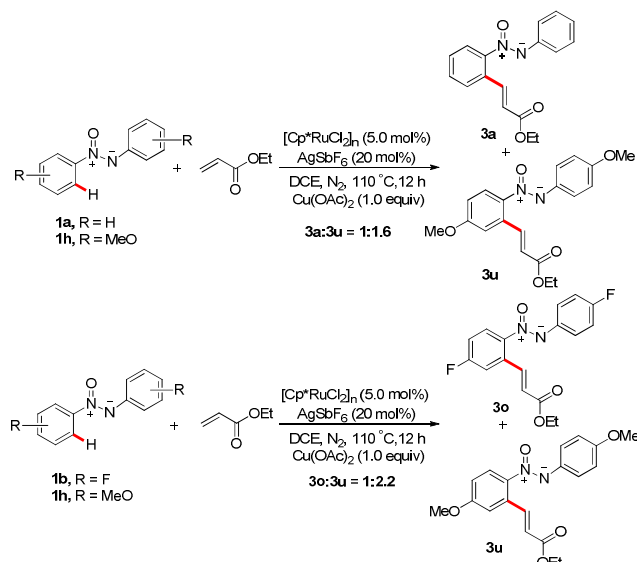


<sup>a</sup> Reaction conditions: azoxybenzene (**1**, 0.20 mmol), alkene (**2**, 0.30 mmol), [Cp\*RuCl<sub>2</sub>]<sub>n</sub> (5.0 mol%), AgSbF<sub>6</sub> (0.04 mmol) Cu(OAc)<sub>2</sub> (0.20 mmol), DCE (1.0 mL), 110 °C, N<sub>2</sub>, 12 h. <sup>b</sup> Isolated yields. <sup>c</sup> 130 °C.

**Scheme 3.** The alkenylation of azoxybenzenes with alkenes<sup>a</sup>

Subsequently, the optimization of reaction time and temperature did not improve the yield of product **3a** (Table 1, entries 8–11). When the molar ratio of **1a/2a** (1:2) was controlled, lower yield of **3a** was achieved (41%), and the formation of disubstituted product may account for this result (Table 1, entry 12).<sup>13</sup> It was found that the use of silver salt as additive resulted into lower yields of **3a** (Table 1, entries 13 and 14). Additionally, it was found that the Ru-catalyzed alkenylation reaction could not proceed in the absence of Cu(OAc)<sub>2</sub> (Table 1, entries 15 and 16). Finally, some typical reaction media were investigated and experiment results indicated that DCE was the most suitable solvent in this reaction (Table S1 in Supporting Information).

With the optimized reaction conditions in hand, we next explored the substrate scope in Ru-catalyzed alkenylation of

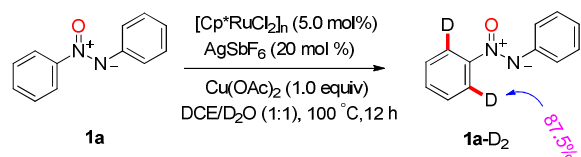


**Scheme 4.** Intermolecular competition experiments

azoxybenzenes **1** with alkenes **2**, as shown in Scheme 3. Under nitrogen atmosphere, a variety of alkyl acrylates reacted with azoxybenzene **1a** smoothly under present reaction conditions, and the corresponding products **3a–h** were isolated in 57–81% yields. Generally, alkyl acrylates with low boiling point would lead to much lower yields of the desired products (**3a–c** vs **3d–h**). When 2-hydroxyethyl acrylate **2i** was used to couple with **1a**, the corresponding olefinated product **3i** was isolated only in 29% yield, even at elevated temperature. On the other hand, aryl acrylates (**2j–l**) were used the coupling partners in the alkenylation of **1a**, providing the anticipated products (**3j–l**) in satisfactory yields. Interestingly, the reactions of diethyl and dimethyl vinylphosphonates with **1a** generated the coupling products **3m** in 65% yield, and **3n** in 59% yield, respectively. Next, the scope of azoxybenzenes was also examined using ethyl acrylate as one of the coupling partner. Electron-withdrawing groups (F, Cl, and CO<sub>2</sub>Et) and electron-donating groups (Me, and MeO) at the *para*-positions of the nitrogen on the benzene rings were all tolerated under the optimized reaction conditions. In the most cases, electron-rich azoxybenzenes seemed to be more active than that electron-deficient one, and the former gave slightly high yields of the corresponding products (**3q** vs **3u**). Moreover, the steric effect was distinctively observed when methyl-substituted azoxybenzenes at their *para*-, *meta*- and *ortho*-positions were used to react with ethyl acrylate, giving the products **3r–t** in 67%, 60% and 33% yields, respectively.

Next, we focused on the intermolecular competition experiments,<sup>5a,14</sup> which were performed using differently substituted azoxybenzenes and ethyl acrylate under standard reaction conditions, as shown in Scheme 4. The experimental results revealed that electron-rich azoxybenzene was preferentially functionalized in C–H activation, and high yields of the corresponding products were obtained (Scheme 4).

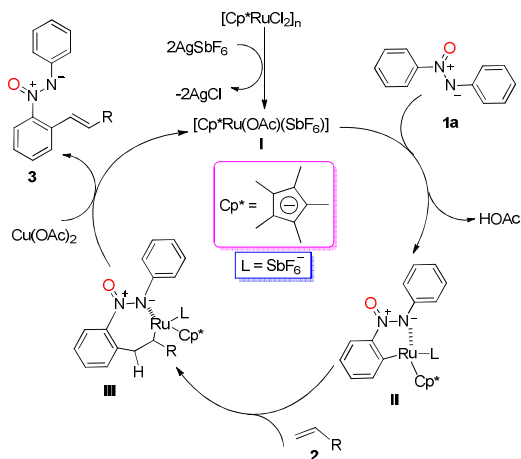
In addition, we continued our investigation into selective H/D exchange<sup>15</sup> at the *ortho*-positions of azoxy group on the benzene ring, which was performed in the mixture of DCE/D<sub>2</sub>O (1:1) at 110 °C under nitrogen atmosphere for 12 h (Scheme 5). A



**Scheme 5.** Ru<sup>III</sup>-catalyzed *ortho*-selective alkenylation

significant D/H exchange (87.5%) provided the solid evidence for a reversible C–H bond ruthenation process.

Building on the above experiment results and known Ru-catalyzed C–H bond activation,<sup>5,14,15</sup> a possible reaction mechanism is described in Scheme 6. Firstly, the anion exchange of AgSbF<sub>6</sub> with [Cp\*RuCl<sub>2</sub>]<sub>n</sub> generated Ru<sup>III</sup> species **I**, which reacted with **1a** to form a five-membered metallacycle **II** by Ru-catalyzed *ortho*-selective C–H bond activation of **1a** and its coordination. Then, the coordinative insertion of alkene **2** into intermediate **II** afforded a seven-membered intermediate **III**. Finally, the β-hydrogen elimination from intermediate **III** gave the final product **3** and regenerated the active ruthenium species **I** for next run. Although the exact role of the Cu<sup>II</sup> salt was not clear, we proposed that the acetate anion maybe coordinate to the ruthenium species and accelerate the *ortho*-metalation.<sup>14b</sup>



**Scheme 6.** The proposed reaction mechanism

In conclusion, we have developed a highly selective Ru<sup>III</sup>-complex-catalyzed *ortho*-alkenylation of azoxybenzenes with activated alkenes in the presence of AgSbF<sub>6</sub> and Cu(OAc)<sub>2</sub> to afford a variety of olefinated azoxy derivatives in good yields. Further application of these useful azoxy compounds and detailed mechanistic investigation are in progress.

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## Notes and reference

<sup>a</sup> Department of Chemistry, Huaibei Normal University, Huaibei, Anhui 235000, P R China; E-mail: leiwang@chnu.edu.cn  
Tel.: +86-561-380-2069; fax: +86-561-309-0518

<sup>b</sup> State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P R China

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