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Cp*Rh(III) and Cp*Ir(III)-Catalysed Redox-Neutral C-H

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Cp*Rh(III) and Cp*Ir(III)-catalysed direct C-H arylation with quinone diazides as efficient coupling partners is disclosed. This redox-neutral protocol offers a facile, operationally simple and environmentally benign access to arylated phenols. The reaction represents the first example of Cp*Ir(III)-catalysed C-H direct arylation reaction.

of Arylated Phenols

The biaryl scaffold is prevalent in numerous functional molecules. Conventionally, the transition metal-catalysed cross coupling reaction provides a reliable strategy for biaryl synthesis.^[1] Recently, with the advent and great advances of metal-catalyzed C-H activation reaction,^[2] direct C-H arylation offers a more straightforward and atom-economic pathway for their synthesis.^[3] Cp*Rh(III) are among the most attractive catalysts which enable the functionalization of various C-H bonds to furnish diverse C-C and C-heteroatom bonds under typically mild reaction conditions and with low catalyst loading.^[4] In the context of C-H arylation reaction, however, only limited examples exist (Scheme 1a).[5-10] For instance, it has been demonstrated that Cp*Rh(III) could promote the dehydrogenative coupling of two distinct arenes in an intramolecular^[5] or intermolecular^[6] manner via dual C-H activation. Though elegant, these reactions usually occur under drastic reaction conditions. And for intermolecular reactions, a large excess of one arene is typically needed. In addition, several examples of oxidative C-H coupling reactions with aryl organometallic reagents, namely arylboronic acids^[7] and arylsilanes^[8] were reported, with large amount of oxidants Ag⁺ and/or Cu²⁺ salt necessitated. Interestingly, it is only very recently that aryl iodides are identified as efficient coupling partners for Rh(III)-catalyzed arylation of anilides.^[9] Aside from these examples, Li realized an alternative C-H arylation reaction via an interesting formal Michael addition/rearomatization pathways by using 4-hydroxycyclohexa-2,5-dienones as the arylating reagents (Scheme 1b).^[10] Herein, we report our realization of a mild Cp*Rh(III) and Cp*Ir(III)-catalyzed C-H arylation with quinone diazides to furnish arylated phenols^[11] under simple and redox-neutral reaction conditions. To the best of our knowledge, this is the first example of employing Cp*Ir(III) as catalyst for C-H arylation reaction.^[12,13] It should be noted that phenols are useful

chemical entities. Current C-H arylation reactions are seldom compatible with the phenol functionality due to the oxidative and/or harsh conditions used.

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Our hypothesis was inspired by the recent success of employing diazo compounds as coupling partners in Cp*Rh(III)-catalyzed C-' functionalizations (Scheme 1c).^[14] Structurally, quinone diazides ca. be regarded as carbonyl diazo compounds bearing two electron acceptors.[15,16] Therefore, a Rh-carbenoid was expected to be formed after the C-H activation event. Thereafter, by a subseque. t α -insertion and rearomatization, a direct C-H arylation reaction should be achieved (vide infra for a proposal of mechanism).





c) C-H coupling with diazo compounds

$$H + R^{N_2} \xrightarrow{Cp^*Rh^{|||}}_{ref 14} \xrightarrow{DG}_{[Rh]} \xrightarrow{R'} \xrightarrow{T}_{[Rh]}$$

d) C-H coupling with quinone diazides for arylated phenols synthesis



Scheme 1. Rh(III)-catalyzed biaryl synthesis via C-H functionalization.

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Importantly, quinone diazides are readily synthesized by the diazotization of aminophenols, or by the functionalization of anilines or phenols.^[17]

Initially, we examined the reaction of 2-phenylpyridine **1a** with quinone diazide **2a**. Delightedly, we were able to quickly identify that the reaction proceeded smoothly in the presence of [Cp*RhCl₂]₂ (2.5 mol %), AgSbF₆ (20 mol%) and PivOH (10 mol %) in DCM at 50 °C, giving the desired arylation product **3aa** in 73% yield, along with 17% diarylation product **3aa**' (eq 1). Interestingly, the switch of the catalyst to [Cp*IrCl₂]₂ produced the diarylation product **3aa**' predominately. By increasing the loading of quinone diazide **2a** to 2.5 equivalents, **3aa**' could be obtained in a high yield of 80% (eq 2).



The scope of this transformation was investigated. It was found that the reaction was robust to tolerate various functional groups, giving the corresponding products in generally good to excellent yields (Scheme 2). For para-substituted arenes, significant amounts of diarylation products were usually observed (3aa-3da, 3la, 4ca, 5aa-5ca). However, the meta-substituents could assure a single monoarylation reaction, with the reaction occurring at the less sterically congested positions (3ea-3ga, 4da, 5ea). Notably, orthosubstituents did not hamper the reactivity (3ha, 3ia, 5da). The substituent effect on the pyridine ring was also examined. To our delight, a number of substituents regardless of the electronic properties were well tolerated (3ja-3na). We would like to point out that 6-methoxypyridin-2-yl (3ja) and 3-methylpyridin-2-yl (3na), which are potentially difficult directing groups due to the steric hindrance, effected the reaction smoothly. 2-(Naphthalen-2yl)pyridine was arylated exclusively at the β-position in 86% yield (3oa). Benzo[h]quinolone was also a suitable substrate (3pa). Apart from pyridinyl, pyrazolyl (4ca, 4da) and pyrimidyl (5aa-5fa) groups were also effective chelating groups for this transformation.

We then investigated the substrate scope of quinone diazides (Scheme 3). With 2-(*m*-tolyl)pyrimidine as substrate, we were delighted to find that the reaction was compatible not only with *para*-quinone diazides (**5ea-5ed**), but also with *ortho*-quinone diazides (**5ee-5eh**). Thus, a variety of quinone diazides with different substituents proceeded smoothly, giving the arylation products in moderate to good yields. The survival of halides like Cl and Br provided opportunities for further functionalization.

Due to the important utility of extended π -conjugated compounds in materials, we further evaluated the substrate scope for the formation of bis-functionalization products (Scheme 4). Again, different substrates bearing a N-heterocyclic directing group such as pyridinyl, pyrazolyl and pyrimidyl underwent reaction without difficulties. Notably, the hydroxymethyl group was also tolerated, suggesting the mildness of this reaction (**4ba'**). It should be noted the biheteroaryl 1-(thiophen-3-yl)-1*H*-pyrazole also delivered the diarylation products in excellent yield (**4fa'**). The electron-

withdrawing CF₃ retarded the reaction, giving **5ca'** in only 28% yield.



Scheme 2. Cp*Rh(III)-catalysed C–H arylation of different arenes with quinone diazide **2a**.^[a] monoarylation: diarylation ratio.



Scheme 3. Cp*Rh(III)-catalysed C–H arylation with various quinor diazides.

To further expand the scope of this reaction, we turned our attention to the arylation of indoles and pyroles (Scheme 5). Indoand pyroles frequently occur in biologically active compounds. By installing a pyrimidyl directing group, the reaction of 1-(pyrimidin 2-yl)-1*H*-indole with **2a** worked effectively in the presence of eith r Cp*Rh(III) or Cp*Ir(III) catalyst, with Cp*Ir(III) giving slightly higher yield (**6aa**). The reaction efficiency was thus evaluated und the catalysis of Cp*Ir(III). Delightedly, various indoles bearing. Page 3 of 4

different substituents at different positions were suitable substrates for this transformation. Of note, the β -methyl substituted indole also delivered the arylation product in moderate yield (**6ia**). Unfortunately, the biheterocyclic 1*H*-pyrrolo[2,3-c]pyridine showed no reactivity in this reaction (**6ja**). Importantly, pyroles were also suitable substrates for this transformation, although the 2-formyl pyrole substrate gave a yield of only 27% (**7ba**).



Scheme 4. Cp*Ir(III)-catalysed C-H diarylation reaction with 2a.



Scheme 5. Cp*Ir(III)-catalysed C–H arylation of indoles and pyroles. ^[a] Cp*Rh(III) was used instead of Cp*Ir(III).

The exposure of 4-chlorobenzenediazonium chloride to the reaction led to no desired arylation product, indicating the importance of the quinone moiety for this reaction (eq 3). A kinetic isotope effect value of 1.1 was observed, which suggests the C–H activation is not involved in the rate-determining step (eq 4).^[18]

control experiments



On the basis of these experiments and literature precedents, γ proposed mechanism was outlined in scheme 6. The active Cp*Rh(III) or Cp*Ir(III) catalyst is generated by ligand exchang γ with PivOH. C–H activation under the assistance of *N*-containing hetercyclic directing group delivers a cyclometallated intermediate **L**. According to our KIE experiments, this step promoted by Cp*Rh(III) catalyst is not involved in the rate-determining step reacts with quinone diazide to form a metal carbene species **B** with the extrusion of N₂. The subsequent migratory insertion furnion intermediate **C**. Upon protonation with PivOH, **D** was produced and the catalyst is regenerated. The aromatization of intermediate **D** gives the final arylated product.



Scheme 6. Mechanistic proposal.

In summary, we developed a novel C–H arylation reaction t using quinone diazides as coupling partners. The reaction we efficiently catalysed by Cp*Rh(III) or Cp*Ir(III) catalysts, offering o quick and facile access to arylated phenols. Broad substrate scop and good functional group tolerance were observed. To the best of our knowledge, this reaction represents the first example of Cp*Ir(III)-catalysed direct C–H arylation reaction.

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Notes and references

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[†] Electronic Supplementary Information (ESI) available: Experimental procedures, structural proofs, spectral data, and mechanistic studies are provided. See DOI: 10.1039/b000000x/

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