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Oxidant-Free Rh(III)-Catalyzed Direct C−H Olefination of Arenes with Allyl Acetates

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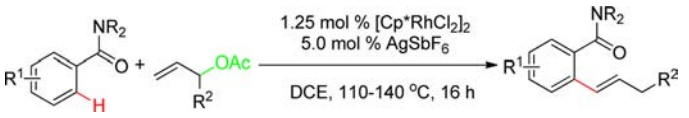
ABSTRACT



Rh(III)-catalyzed direct olefination of arenes with allyl acetate *via* C−H bond activation is described using *N,N*-disubstituted aminocarbonyl as the directing group. The catalyst undergoes a redox neutral process, and high to excellent yields of *trans*-products are obtained. This protocol exhibits a wide spectrum of functionality compatibility because of the simple reaction conditions employed and provides a highly effective synthetic method in the realm of C−H olefination.

Over the past decades, transition-metal-catalyzed oxidative olefination of arenes through direct C−H bond activation has been demonstrated to be an effective and efficient synthetic protocol for introducing an alkene moiety (Scheme 1, eq 1).[1] A diversity of arene C−H olefinations catalyzed by different transition metals has been reported.[2] The use of *ortho*-directing groups (DG), such as imino,[3] 2- imidazolyl,[4] carbonyl,[5] amido,[6] hydroxyl,[7] and 2-substituted pyridyl[8] have been commonly adopted to improve the regioselectivity as well as reaction efficiency of the reaction. Theoretically, an oxidant is needed to regenerate the active catalyst. However, the forced use of external oxidants provides relatively harsh reaction conditions and produces stoichiometric amounts of related heavy metal wastes.

In the arena of C−H activation, one emerging strategy is the use of entities which act as both DG and internal oxidants (DG^{Ox}) at the same time (eq 2). Some traditional directing groups, *N*-oxides,[9] oxime ester, and *N*-methoxyamides,[10] were found to play a dual role in such an olefination process. The Pd-catalyzed olefination of quinoline-*N*-oxides reported by Cui and Wu[11] gives the idea that cleavage of N−O bonds can act as both an inducing platform and an oxidant in the olefination reaction. Although the reaction required a high reaction temperature,

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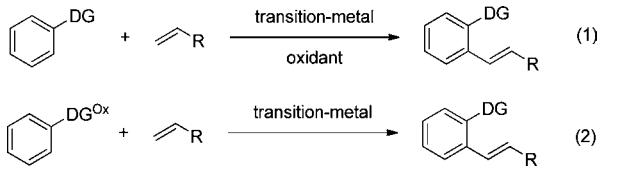
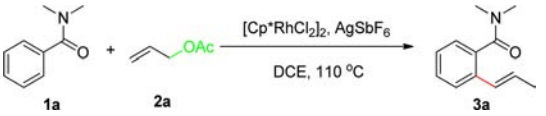
Scheme 1. Transition-Metal-Catalyzed Oxidative Olefination



it proposed the possibility of improving the atom efficiency and decreasing toxic waste formation. Recently, Fagnou et al. reported the Rh(III)-catalyzed isoquinoline construction using the N−O bond of *N*-methoxylbenzamide as an inner oxidant.[12] Following this idea, Glorius et al. developed the Rh(III)-catalyzed olefinations, which proceed under mild reaction condition and tolerate a broad range of functionalities.[13] Meanwhile, an interesting allylation of arenes was disclosed by Ellman, using allyl acetate as the coupling partner.[14] Although a substoichiometric amount of $Cu(OAc)_2$ is still needed to maintain the yield, this finding did invoke the possibility of oxidant-free C−H olefination. With our continuing interest in Rh-catalysis[15] and to discover a new protocol in the realm of C−H olefination, we would like to report, herein, the Rh(III)-catalyzed C−H olefination reaction of *N,N*-disubstituted benzamide with allyl acetate without any external oxidants.[16]

Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	additive	solvent	yield[b] (%)
1	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DME	62
2	$[Cp^*RhCl_2]_2$	$AgSbF_6$	dioxane	58
3	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	92
4	$[Cp^*RhCl_2]_2$	$AgSbF_6$	THF	74
5	$[Cp^*RhCl_2]_2$	$AgSbF_6$	*t*-AmOH	53
6	$[Cp^*RhCl_2]_2$	$AgSbF_6$	acetone	80
7	$[Cp^*RhCl_2]_2$	$AgSbF_6$	MeCN	NR
8	$[Cp^*RhCl_2]_2$	AgOAc	DCE	NR
9	$[Cp^*RhCl_2]_2$	–	DME	NR
10	–	$AgSbF_6$	DME	NR
11	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DME	NR[c]

[a] Unless otherwise noted the reactions were carried out at 110 °C using **1a** (0.2 mmol), **2a** (0.24 mmol), catalyst (0.0025 mmol), and additive (0.01 mmol) in solvent (1 mL) stirred for 16 h. [b] Isolated yields. [c] K_2CO_3 (0.2 mmol) was added. DCE = 1,2-dichloroethane, DME = 1,2-dimethoxylethane.

At the outset of our studies, the reaction conditions were optimized using *N,N*-dimethylbenzamide (**1a**) and allyl acetate (**2a**) as the model substrates. After extensive trials, we were pleased to find that 62% yield of the desired olefination product could be obtained. Guided by the dramatic solvent effect observed in our previous work, a series of solvents were subsequently examined and 1,2-dichloroethane proved to be the optimal choice (Table 1, entries 1−7).[15] Much to our surprise, when AgOAc was added instead of $AgSbF_6$, no reaction occurred, which indicates the vital importance of a cationic rhodium catalyst in the catalytic cycle (Table 1, entry 8). Not surprisingly, the reaction did not proceed in the absence of either the Rh(III) catalyst or silver additive (Table 1, entries 9, 10). In addition, when a stoichiometric amount of K_2CO_3 was added, the reaction was totally suppressed (Table 1, entry 11).

With the optimized reaction condition in hand, we turned our attention to the exploration of the reaction scope of various *N,N*-disubstituted benzamide derivatives with allyl acetate (**2a**) as the model coupling partner. Both electron-donating and -withdrawing functional groups at the *para*-position of *N,N*-dimethyl amide group were well adapted in this reaction, and corresponding olefination products were obtained in high yields (Scheme 2, **3b**−**3l**). Notably, methoxy (**3c**), TMS (**3d**), trifluoromethyl (**3e**), bromo (**3i**), acetal (**3j**), and ester (**3k**), which are valuable functional groups amenable for further derivatization, were all well tolerated. 2-Naphthamide was also a suitable substrate, giving the *C*3-olefination product in 82% yield (Scheme 2, **3m**). As HOAc is formed in this catalytic cycle,

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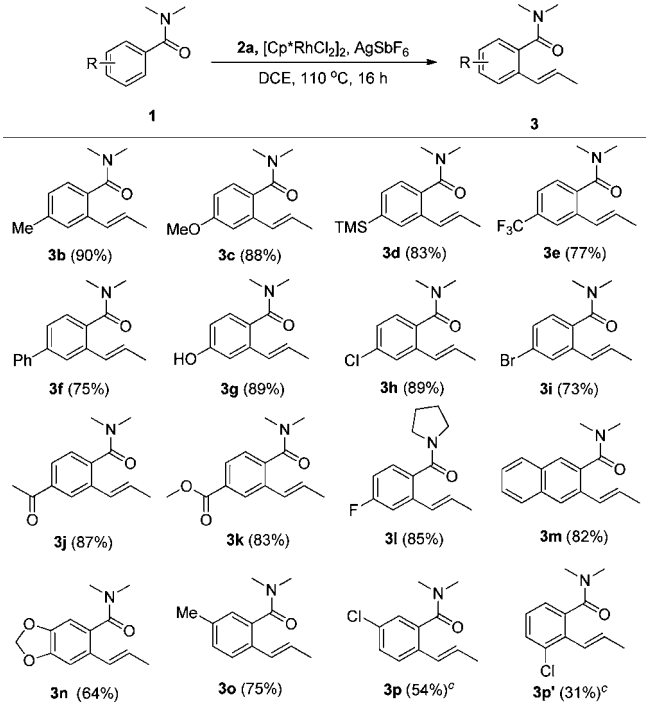
(16) While preparing our manuscript, Glorius et al. reported a similar protocol for Rh(III)-catalyzed direct C−H allylation of arenes using allyl carbonates: Wang, H.; Schröder, N.; Glorius, F. *Angew. Chem., Int. Ed.* **2013**, *52*, 5386.

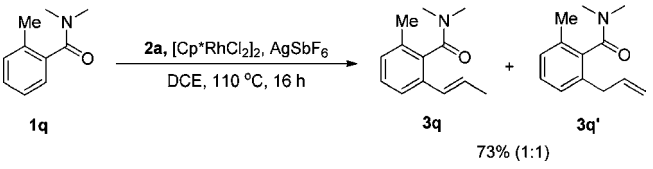
the weak acidity of the reaction media would lead to decomposition of the dioxole group, which gave a moderate yield of 64% (Scheme 2, **3n**). With regard to a *meta*-methyl substituted substrate, the reaction selectively happened at a sterically more accessible site, thus delivering the desired product in high yield (Scheme 2, **3o**). However, for the *meta*-Cl substituted analogue, the reaction tended to afford a mixture of two regioisomers (Scheme 2, **3p**, **3p′**). When an *ortho*-methyl substituted *N,N*-dimethylbenzamide substrate was engaged in such an olefination reaction, a mixture of the allylation product and alkenylation products was obtained with an isomeric ratio of 1:1 (Scheme 3).

Scheme 2. Scope of *N,N*-Dimethylbenzamide Derivatives[a,b]



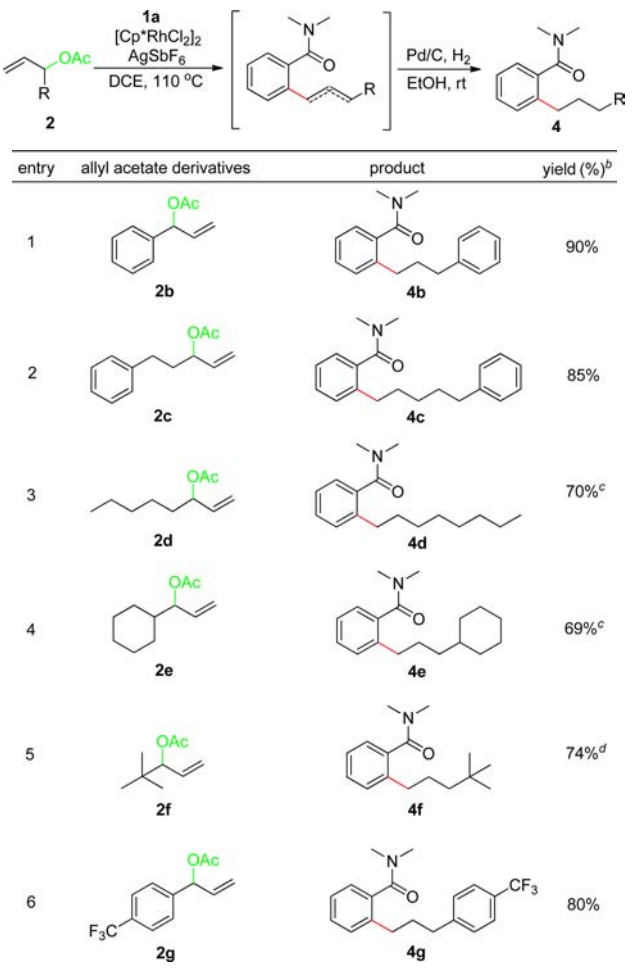
[a] Unless otherwise noted the reactions were carried out at 110 °C using **1a** (0.2 mmol), **2a** (0.24 mmol), $[Cp^*RhCl_2]_2$ (0.0025 mmol), $AgSbF_6$ (0.01 mmol) in DCE (1 mL) stirred for 16 h. [b] Isolated yields. [c] Catalyst (0.005 mmol) was used. DCE = 1,2-dichloroethane.

Scheme 3. C−H Olefination of *ortho*-Methyl Substituted *N,N*-Dimethylbenzamide with **2a**[a]



[a] The reactions were carried out at 110 °C using **1q** (0.2 mmol), **2a** (0.24 mmol), $[Cp^*RhCl_2]_2$ (0.005 mmol), and $AgSbF_6$ (0.02 mmol) in DCE (1 mL) stirred for 16 h.

Table 2. Scope of Allyl Acetate Derivatives[a]

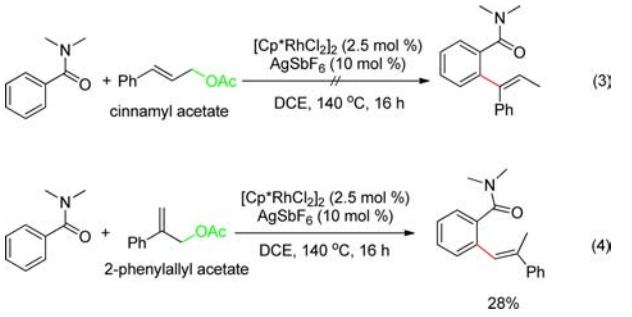


[a] Unless otherwise noted the reactions were carried out at 110 °C using **1a** (0.2 mmol), **2** (0.24 mmol), $[Cp^*RhCl_2]_2$ (0.0025 mmol), and $AgSbF_6$ (0.01 mmol) in DCE (1 mL) stirred for 16 h. [b] Isolated and two-step total yield. [c] $[Cp^*RhCl_2]_2$ (0.005 mmol) and $AgSbF_6$ (0.02 mmol) were used. [d] Reaction temperature is 140 °C.

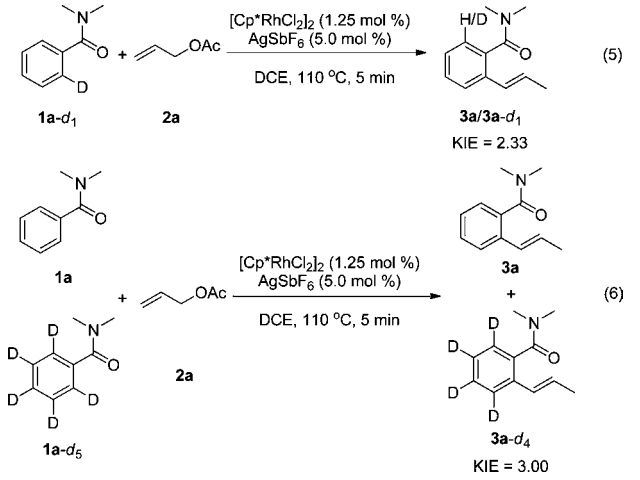
In order to have a better understanding of the protocol, we proceeded to explore the scope of allyl electrophilic partners. While linear allyl acetates, such as cinnamyl acetate, were unreactive, the branched isomer 2-phenylallyl acetate showed good reactivity to afford the *trans* product (Scheme 4). The low yield was attributed to the steric hindrance of the bulky phenyl group. Meanwhile, high yields were obtained with the 1-substituted allyl acetates, of which the products were observed to be mixtures of isomers (Table 2). In order to simplify the characterization of the products, further hydrogenation was adopted. The reaction proceeded readily with complete γ-selectivity, and no terminal alkene product was formed. Compared to aliphatic substituted allyl acetates, those with aromatic substituents afford the desired product in relatively higher yield.

To obtain more detailed information about the mechanism of the present olefination reaction, the following experiments were conducted as shown in Scheme 5. Significant isotope effects were observed in either the intramolecular or intermolecular studies (Scheme 5), thus indicating

Scheme 4. Alkene Counterpart Comparison: Terminal *vs* Internal



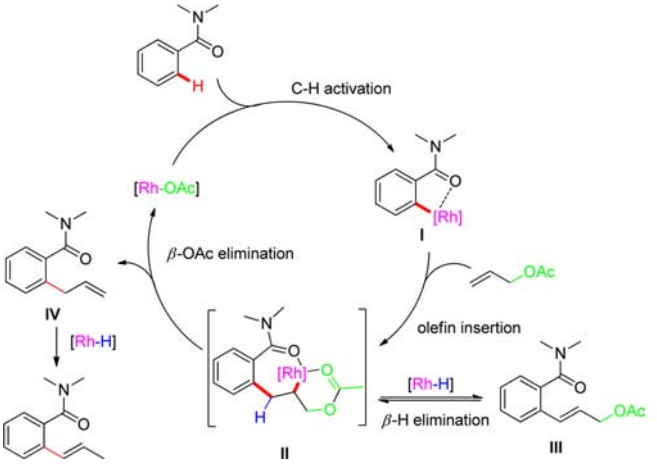
Scheme 5. Kinetic Isotope Effects



the rationality of C−H bond cleavage being the rate-determining step. In combination with the high reactivity of highly electron-deficient substrates, a concerted-metalation-deprotonation is most likely the plausible mechanistic pathway.

On the basis of our experimental results, a plausible mechanism is proposed in Scheme 6. Precomplexation of the amide substrate with an active Rh(III) catalyst would trigger *ortho* C−H bond activation to form the metallacycle *via* a concerted-metalation-deprotonation pathway to deliver the intermediate **I**. After migratory insertion by the incoming alkene, a seven-membered Rh(III) species **II** is formed with carbonate oxygen chelating to the metal. Then β-acetate elimination[17] would happen to give the

Scheme 6. Plausible Catalytic Mechanism



product **IV** and regenerate the active Rh(III) catalyst. The final product is obtained after the migratory isomerization of the double bond, which may due to the effect of trace [Rh−H] complex. Due to the conformational restriction, the β-hydride elimination with the benzylic H-atom would be prevented by the coordination of the directing group. During the whole catalytic cycle, the Rh(III) catalyst undergoes a redox neutral process, which indicates an oxidant-free strategy with the acetate anion as a leaving group.

In conclusion, we have reported a novel cationic Rh(III)-catalyzed olefination of *N,N*-disubstituted benzamides with allyl acetate derivatives, which delivers *trans*-products in high to excellent yields without the need for an external oxidant. The ambient condition and high efficiency of this reaction shows tolerance of a range of functionalities.

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Supporting Information Available. Additional experimental procedures and full spectroscopy data for all the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.