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A Unique Alkylation of Azobenzenes with Allyl Acetates by Rh^{III}-Catalyzed C−H Functionalization

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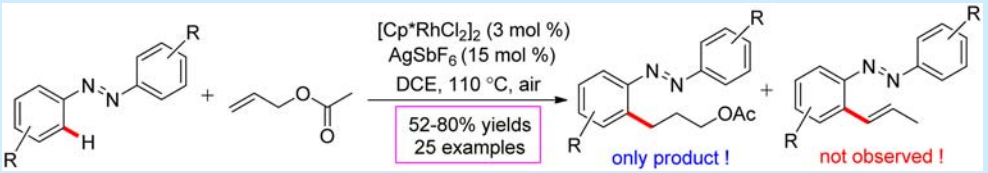
Supporting Information

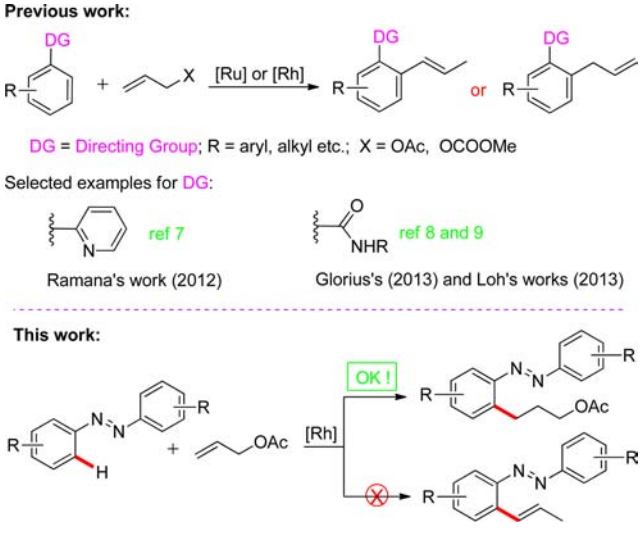


ABSTRACT: A novel Rh^{III}-catalyzed direct alkylation of azobenzenes with allyl acetates through C−H activation and functionalization is demonstrated in which the allyl acetates serve as unique alkylation agents. The rhodium-catalyzed alkylation provides a highly efficient and atom-economic approach to a series of azo compounds.

In recent years, the direct functionalization of inert C−H bonds in the presence of transition-metal catalyst has become an attractive strategy in synthetic organic chemistry.[1] Traditionally, these transition metals based on copper, palladium, ruthenium, and rhodium complexes have been found to facilitate C−C bond formation.[2] Among them, Rh salts and related complexes behaved with higher activity and had been successfully applied in the group-directing C(sp^2)−H functionalization.[3] Allyl acetate, as a popular and important allylation reagent, has been frequently investigated in organic transformations.[4] However, it was found that allyl acetate and its derivatives in early reports generally produced allyl or olefinated arenes.[5] These reactions mainly include transition-metal-catalyzed cross-coupling reactions,[5a−f] Lewis acid catalyzed (or promoted) Friedel−Crafts allylation of electronic-rich arenes,[5g,h] and catalytic C−H activation of electron-deficient arenes.[5i−p] More recently, Ellman and co-workers reported a direct allylation of arenes by using allyl acetate as coupling partner.[6] Ramana et al. reported a Ru-catalyzed allylation of 2-phenylpyridine.[7] Glorius realized the first Rh^{III}-catalyzed direct C−H allylation of arenes with allyl carbonates (Scheme 1).[8] Meanwhile, Loh's group developed a Rh^{III}-catalyzed intermolecular C−H olefination of arenes with allyl acetates under oxidant-free conditions (Scheme 1).[9] Although these works have made breakthroughs in allylation reactions, double bond migration and poor regioselectivity were inevitable and not easily controlled. Hence, exploring more efficient and new reaction patterns of allyl acetates to construct useful compounds is highly desirable.

Aromatic azo compounds have received much attention for their unique properties[10] and wide applications.[11] Recently, our group utilized azobenzene as a new directing group to realize *ortho*-C−H functionalization,[12] which expanded the synthesis of steric azo compounds. On the basis of these findings, we envision that aromatic azo compounds would interact with transition metals to form an active species, which could enable possible cross-coupling. Inspired by elegant works on Rh catalysis,[13] we attempted a reaction of allyl acetates with azobenzenes in the presence of $[Cp^*RhCl_2]_2$ as catalyst and $AgSbF_6$ as additive. To our surprise, only alkylated products of azobenzenes were observed, and no olefinated products were found. This finding is quite different from Glorius' and Loh's results.[8,9] Herein, we report this novel Rh-catalyzed direct C−H alkylation of azobenzenes with allyl acetates (Scheme 1).

Scheme 1. Transition Metal-Catalyzed Alkylation and Allylation



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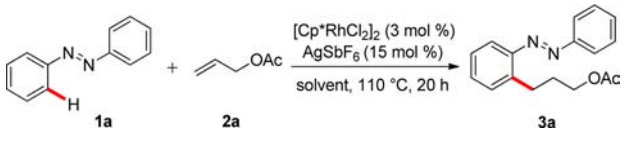
A feasible alkylation was first investigated using azobenzene (**1a**) with allyl acetate (**2a**) in the presence of $AgSbF_6$ and $[Cp^*RhCl_2]_2$, as shown in Table 1. To our delight, 69% of

Table 1. Optimization of the Reaction Conditions[a]



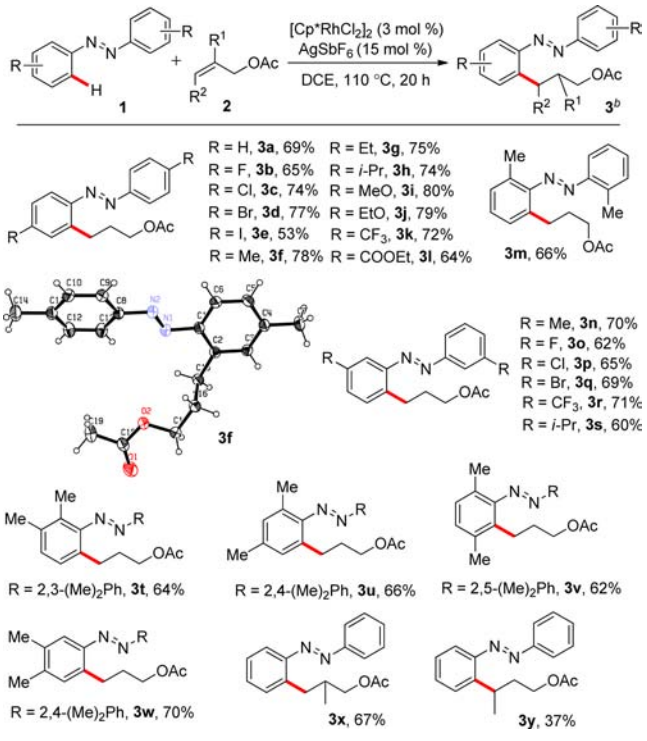
entry	catalyst	additive	solvent	yield[b] (%)
1	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	69
2	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	46[c]
3	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	69[d]
4	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	70[e]
5	$[Cp^*RhCl_2]_2$	$AgSbF_6$	DCE	71[f]
6	$[Cp^*RhCl_2]_2$	K_3PF_6	DCE	trace
7	$[Cp^*RhCl_2]_2$	$NaBF_4$	DCE	n.r.
8	$[Cp^*RhCl_2]_2$	$AgSbF_6$	THF	n.r.
9	$[Cp^*RhCl_2]_2$	$AgSbF_6$	dioxane	41
10	$[Cp^*RhCl_2]_2$	$AgSbF_6$	toluene	27
11	$[Cp^*RhCl_2]_2$	$AgSbF_6$	HOAc	trace
12	$[Cp^*RhCl_2]_2$	$AgSbF_6$	CH_3CN	30

[a]Reaction conditions: azobenzene (**1a**, 0.40 mmol), allyl acetate (**2a**, 0.30 mmol), $[Cp^*RhCl_2]_2$ (3 mol %), additive (15 mol %), solvent (1.0 mL) at 100 °C in air for 20. [b]Isolated yield. [c]$AgSbF_6$ (10 mol %). [d]$AgSbF_6$ (20 mol %). [e]100 °C. [f]110 °C. Cp* = pentamethylcyclopentadienyl. n.r. = no reaction.

desired product **3a** was isolated in the presence of $[Cp^*RhCl_2]_2$ (3 mol %) and $AgSbF_6$ (15 mol %) in 1,2-dichloroethane (DCE) as solvent at 110 °C for 20 h (entry 1). Additionally, we found that only 46% of **3a** was formed when 10 mol % of $AgSbF_6$ was employed (entry 2). Improvement of **3a** yield by increasing the amount of $AgSbF_6$ from 10 mol % to 20 mol % failed (entry 3). Changing the reaction temperature did not improve the yield of **3a** (entries 4 and 5). When $AgSbF_6$ was replaced with K_3PF_6 or $NaBF_4$, no product **3a** was obtained, and starting materials were recovered (entries 6 and 7). Subsequently, a series of solvents, such as tetrahydrofuran (THF), dioxane, toluene, HOAc, and CH_3CN, were examined, but no increased yield of **3a** was achieved (entries 8–12).

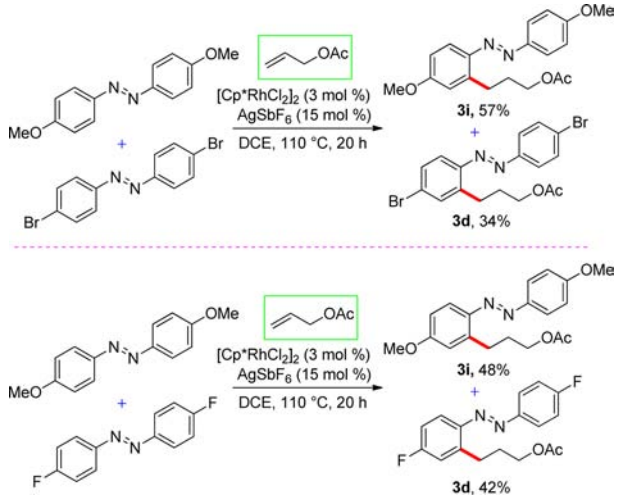
After achieving the optimal alkylation conditions, we further explored the scope of azobenzenes and allyl acetates in this $C(sp^2)$–$C(sp^3)$ bond-forming protocol. As shown in Scheme 2, a variety of structurally diverse azo compounds underwent efficient alkylation with allyl acetate (**2a**), as a representative partner, to generate the corresponding products in good yields with excellent regioselectivity. With the exception of the iodide, the azobenzenes bearing other halogens (F, Cl, and Br) at the *para* positions afforded the desired products (**3b–d**) in good yields. Meanwhile, the azobenzenes with the *para*-substituted groups, including electron-donating and electron-withdrawing ones (alkyl, alkoxyl, trifluoromethyl, and ester), delivered the desired products (**3f–l**) in 64–80% yields. The excellent selectivity was further supported by the X-ray single crystal structure analysis of **3f**. Notably, electron-donating group seems to be more helpful on the transformations (**3f–j** vs **3k–l**), and the intermolecular competing experiments also gave similar results (Scheme 3). Additionally, no obvious steric hindrance was observed regardless of the electronic nature and size of the substituent (**3a** vs **3l**, **3f** vs **3m**). Most of the *meta*-substituted azobenzenes led to smooth alkylation, affording desired

Scheme 2. Scope of Azobenzenes and Allyl Acetates[a]



[a]Reaction conditions: azobenzene (**1**, 0.40 mmol), allyl acetate (**2**, 0.30 mmol), $[Cp^*RhCl_2]_2$ (3 mol %), $AgSbF_6$ (15 mol %), DCE (1.0 mL) at 110 °C in air for 20 h. [b]Isolated yield.

Scheme 3. Intermolecular Competing Experiments



products (**3n–s**) in 60–71% yields. In addition to monosubstituted azobenzenes, those with disubstituted groups also could generate the alkylated products (**3t–w**) in good yields and with no observable olefination product. It was found that 2-methylallyl acetate gave the corresponding product **3x** in 67% yield, and crotyl acetate gave **3y** in 37% yield. However, no product was obtained when cinnamyl acetate, styrene, allyl carbonate, allyl ether, or allyl amine reacted with **1a**. Employing an excess of allyl acetate (**2a**) in the alkylation of (*E*)-1,2-bis(2,3-dimethylphenyl)diazene allowed the generation of disubstituted product **3w′** in 52% yield along with a trace amount of **3w** (Scheme 4).

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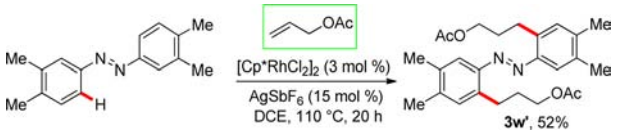
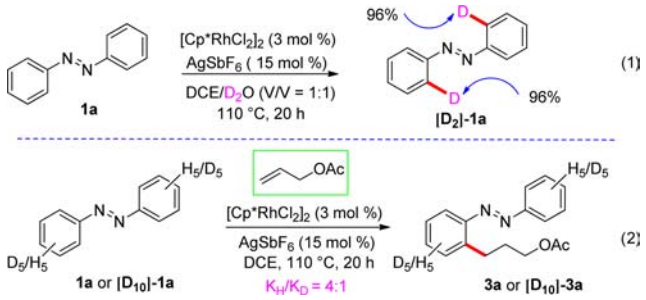
Scheme 4. Selective Dialkylation Reaction



Subsequently, we turned our attention to investigate the preliminary mechanism of the alkylation of azobenzene with allyl acetate. As revealed in Scheme 5, when **1a** was subjected to

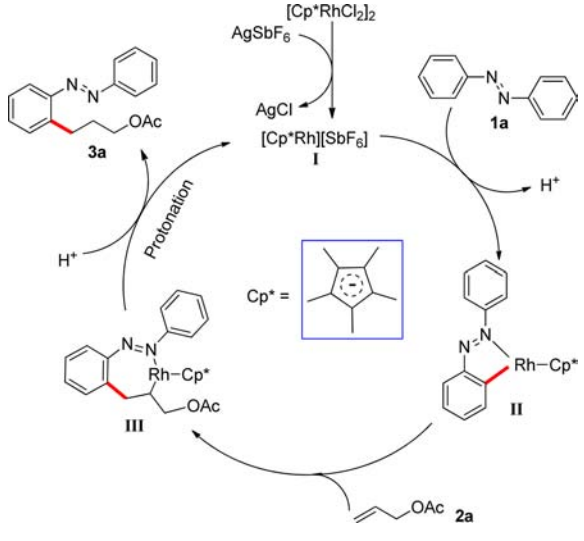
Scheme 5. H/D Exchange and Kinetic Isotope Effect (KIE) Experiments



DCE/D_2O (v/v = 1:1) in the presence of $[Cp^*RhCl_2]_2$ (3 mol %) and $AgSbF_6$ (15 mol %), a D/H ratio was observed and determined as 96% through ^1H NMR analysis (eq 1, Scheme 5; see the Supporting Information for details). Furthermore, a significant isotope effect was also found in intermolecular investigations (eq 2, Scheme 5). These results indicated that C−H cleavage is irreversible and may be involved in the rate-determining step.

According to our preliminary mechanistic studies and Rh catalysis,[14] a possible alkylation process is proposed in Scheme 6. The alkylation mechanism begins with anion exchange between $[Cp^*RhCl_2]_2$ and $AgSbF_6$, affording an active species **I**.[15] Then azobenzene (**1a**) reacts with **I** to generate a cyclorhodium intermediate **II** through Rh^{III}-catalyzed *ortho*-C−H bond activation of **1a** and its coordination. The insertion of formed **II** into allyl acetate (**2a**) leads to the formation of

Scheme 6. Proposed Reaction Mechanism



intermediate **III**. Finally, a protonolysis of **III** releases the product **3a** and regenerates **I** for the next catalytic cycle.

In conclusion, we have developed a unique alkylation of azobenzenes with allyl acetates through Rh catalysis under air. This process provides an efficient protocol for the synthesis of a series of *ortho*-alkylated azobenzenes. To the best of our knowledge, this is the first example of Rh-catalyzed direct alkylation of azo compounds. Further studies focusing on the reaction mechanism and the product applications are currently under investigation.

■ ASSOCIATED CONTENT

Supporting Information

Full experimental details and characterization data for all products. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b00957.

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Notes

The authors declare no competing financial interest.

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