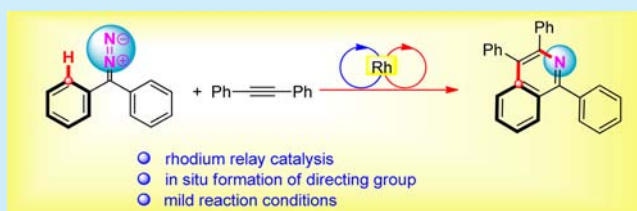


Realized C–H Functionalization of Aryldiazo Compounds via Rhodium Relay Catalysis

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Supporting Information

ABSTRACT: An unprecedented C–H functionalization of aryldiazo compounds without a preinstallation of directing group has been realized under mild conditions, which differs from former reports in its use of diazo compounds as coupling partners in directed C–H activations. This novel transformation has been realized by a rhodium self-relay catalysis, a tandem process of the in situ formation of a directing group and sequential C–H bond activation.

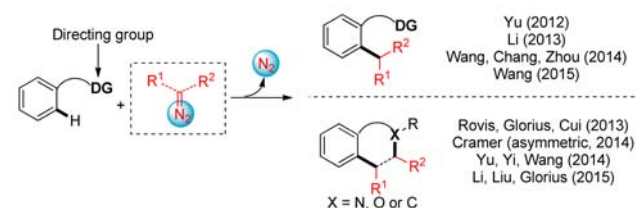


Transition-metal catalyzed directed C–H bond functionalization has emerged as a powerful tool for the rapid construction of carbon–carbon, carbon–heteroatom bonds.¹ Generally, a directing-group-containing substrate and functionalized molecules such as alkene, alkyne, which act as coupling partners, are prerequisites.² Meanwhile, as highly reactive precursors, the nature of diazo compounds makes them good coupling partners in C–H activations. In 2011, Wang reported a seminal copper-catalyzed direct benzylation/allylation of 1,3-azoles with *N*-tosylhydrones.³ Later, Yu described the intermolecular cross-coupling of diazomalonates with arene C–H bonds.⁴ Rovis⁵ and Glorius⁶ demonstrated the use of donor/acceptor, acceptor/acceptor diazo compounds in constructing heterocycles, respectively. Pioneered by these elegant works, the diazo-involved C–H activation attracted much attention, and many useful approaches have been developed.⁷ Recently, Li and co-workers designed phenacyl-triethylammonium salts as novel arene substrates for redox-neutral couplings with α -diazo esters via a C–H activation pathway.⁸

Despite this, the published reactions have been limited to the use of diazo compounds as coupling partners by dediazonation and generation of metal carbon species (Scheme 1, A). An intriguing issue is whether the diazo compounds can be employed as the activated targets, not as coupling partners, which, to our knowledge, has not been reported previously. However, the challenges remain: First, how does the directing group appear? Second, the extremely easy decomposition of the diazo moiety in the presence of a late transition metal, especially a rhodium complex, increases the difficulty.⁹ Third, unexpected side reactions are common phenomena in diazo-involved transformations. To circumvent these challenges and continuing with our interest in diazo chemistry,¹⁰ herein we describe the first example of rhodium-catalyzed C–H functionalization of aryldiazo compounds under mild con-

Scheme 1. Diazo-Involved C–H Functionalizations

A. Previous works: diazo compounds served as coupling partner



B. C–H functionalization of diazo compounds (this work):



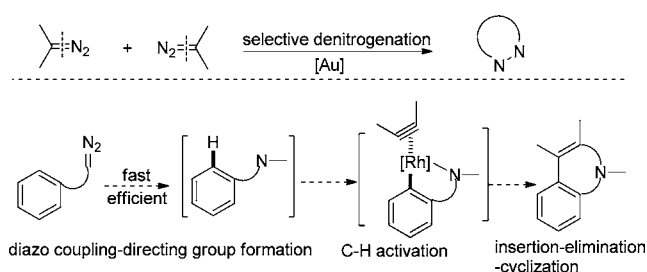
ditions (Scheme 1, B). This novel approach provides a distinct strategy for the formal C–H activation of diazo substrates through in situ formation of a directing group from an active precursor followed by sequential C–H and N–N bond activations.

To address these challenges, a rational strategy needed to be developed. Our former observations on diazo cross-coupling reactions revealed that, through controlling of the reaction parameters, the intermolecular coupling of two diazo compounds could afford *N*-containing intermediates instead of alkenes via selective decomposition one of two diazo moieties (Scheme 2).^{10f} Therefore, we reasoned that the C–H functionalization of the diazo substrate might be realized through a tandem process. Nevertheless, to avoid of unexpected

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Scheme 2. Our Plan toward C–H Functionalization of Diazo Compounds



side reactions, one key concern is that the potential catalytic system should produce the directing-group-containing intermediate in situ rapidly and proceed smoothly to the following C–H activation.

We began our study by utilizing diazo (**1a**) and alkyne (**2a**) as model substrates in the reaction at 80 °C under air (Table 1). Initially, no **3a** was detected when $[\text{Cp}^*\text{RhCl}_2]_2$ (5 mol %) was used in methanol (entry 1). Gratifyingly, 71% yield of **3a**

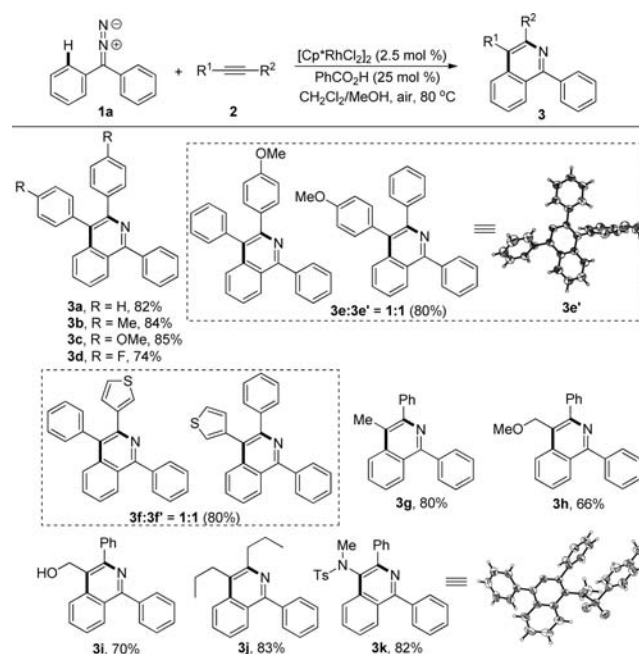
Table 1. Optimization of the Reaction Conditions^a

entry	catalyst	additive	solvent	yield ^b (%)
1	$[\text{Cp}^*\text{RhCl}_2]_2$		MeOH	0
2	$[\text{Cp}^*\text{RhCl}_2]_2$	PhCO_2H	MeOH	71
3	$[\text{Cp}^*\text{RhCl}_2]_2$	PhCO_2H	CH_2Cl_2	0
4	$[\text{Cp}^*\text{RhCl}_2]_2$	PhCO_2H	$(\text{CH}_2)_2\text{Cl}_2$	0
5	$[\text{Cp}^*\text{RhCl}_2]_2$	PhCO_2H	toluene	0
6	$[\text{Cp}^*\text{RhCl}_2]_2$	PhCO_2H	CH_3CN	0
7	$[\text{Cp}^*\text{RhCl}_2]_2$	PhCO_2H	$\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:4)	82
8	$[\text{Cp}^*\text{RhCl}_2]_2$	AcOH	$\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:4)	55
9	$[\text{Cp}^*\text{RhCl}_2]_2$	TsOH	$\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:4)	30
10	$[\text{Cp}^*\text{RhCl}_2]_2$	PivOH	$\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:4)	60
11 ^c	$[\text{Cp}^*\text{RhCl}_2]_2$	$[\text{Ag}]/[\text{Cu}]$	$\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:4)	68
12	$\text{Rh}_2(\text{OAc})_4$	PhCO_2H	$\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:4)	0
13	$\text{Rh}_2(\text{esp})_2$	PhCO_2H	$\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:4)	0
14	$[\text{RhCl}(\text{cod})]_2$	PhCO_2H	$\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:4)	0
15	$\text{Cp}^*\text{Rh}(\text{H}_2\text{O})_3(\text{OTf})_2$	PhCO_2H	$\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:4)	67
16 ^d	$[\text{Cp}^*\text{RhCl}_2]_2$	PhCO_2H	$\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:4)	26
17 ^e	$[\text{Cp}^*\text{RhCl}_2]_2$	PhCO_2H	$\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:4)	82
18 ^f	$[\text{Cp}^*\text{RhCl}_2]_2$	PhCO_2H	$\text{CH}_2\text{Cl}_2/\text{MeOH}$ (1:4)	<5

^aReactions conditions: To a Schlenk tube (10 mL) were added $[\text{Rh}]$ (5 mol %), additive (0.05 mmol), and solvent (5 mL). Then **1a** (0.2 mmol) and **2a** (0.22 mmol) were added under air. The tube was sealed and stirred at 80 °C for 12 h. ^bIsolated yield of **3a**. ^c AgNO_3 (0.04 mmol) and $\text{Cu}(\text{OAc})_2$ (0.2 mmol) were added. ^dPerformed at rt. ^e2.5 mol % of $[\text{Rh}]$. ^fUnder nitrogen.

was obtained when benzoic acid (0.25 eq to **1a**) was added (entry 2), which was further improved to 82% when a mixed solvent ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 1:4) was used. Other solvents such as CH_2Cl_2 , 1,2-dichloroethane, toluene, and acetonitrile did not afford any **3a** (entries 3 to 6). Next, several acids were also examined but gave **3a** in low to moderate yields (entries 8–10). Further screening of rhodium catalysts found that $[\text{Cp}^*\text{RhCl}_2]_2$ remained as the best choice. The use of $\text{Rh}_2(\text{OAc})_4$, $\text{Rh}_2(\text{esp})_2$, and $[\text{RhCl}(\text{cod})]_2$ did not give **3a** at all (entries 12–14), while $\text{Cp}^*\text{Rh}(\text{H}_2\text{O})_3(\text{OTf})_2$ afforded moderate yield (entry 15). The reaction was sluggish when performed at room temperature (entry 16). Moreover, lower catalyst loading still gave **3a** in the same yield (entry 17). However, the yield was very low when performed under nitrogen (entry 18). Interestingly, when an external co-oxidant such as $\text{AgNO}_3/\text{Cu}(\text{OAc})_2$ was used, **3a** was obtained in 68% yield (entry 11).

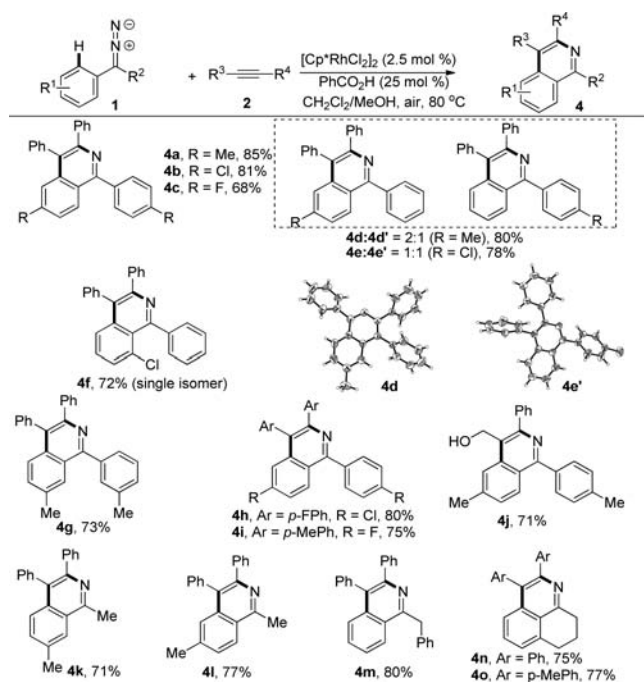
With the optimal reaction conditions in hand, we further investigated the reaction of **1a** with a variety of alkynes (Scheme 3). All of the reactions proceeded well to afford **3** in

Scheme 3. Substrate Scope of Alkynes^{a,b}

^aReaction conditions: **1** (0.2 mmol), **2** (0.22 mmol), PhCO_2H (0.05 mmol), $[\text{Cp}^*\text{RhCl}_2]_2$ (0.005 mmol), CH_2Cl_2 (1 mL), MeOH (4 mL), 80 °C, 12 h. ^bIsolated yields.

moderate to high yields. For the diarylalkynes, the phenyl ring bearing an electron-donating group such as a methyl and methoxy group afforded the corresponding products in higher yields (**3b** and **3c** to **3d**). A similar phenomenon was also observed for dialiphatic-substituted alkyne (**3j**). However, unsymmetric diarylalkynes gave two regioisomers in nearly a 1:1 ratio (**3e/3e'** and **3f/3f'**).¹¹ When the arylalkylalkynes were employed, the desired products were obtained in moderate to high yields with excellent regioselectivities (**3g** and **3h**). Notably, the alkynes bearing a hydroxy group or a *N,N*-tosylmethyl-substituted amine were also tolerated and afforded **3i** and **3k** in 70% and 82% yield, respectively.¹¹

Next, to demonstrate the generality of the reaction, the scope of substrates was further examined. As presented in Scheme 4, the reactions between alkynes and aryl/aryl, aryl/alkyl diazo

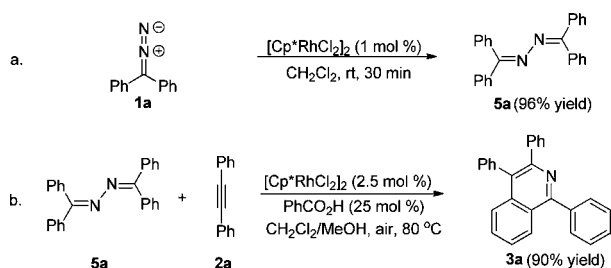
Scheme 4. Substrate Scope^{a,b}

^aReaction conditions: **1** (0.2 mmol), **2** (0.22 mmol), PhCO_2H (0.05 mmol), $[\text{Cp}^*\text{RhCl}_2]_2$ (0.005 mmol), CH_2Cl_2 (1 mL), MeOH (4 mL), 80°C , 12 h. ^bIsolated yields.

compounds proceeded smoothly to furnish the corresponding products in moderate to good yields. Generally, two regioisomers were obtained for unsymmetric diaryl diazo compounds (**4d/4d'**, 2:1 and **4e/4e'**, 1:1),¹¹ while **4f** was isolated as single isomer. The aryl/alkyl diazo compounds were well-tolerated in this reaction, and the desired products were obtained in moderate to high yields (**4k–o**).

The unprecedented directed C–H bond functionalization of aryl diazo compounds prompted us to perform further exploration in order to understanding the reaction process. Thus, control experiments were conducted. First, without the addition of benzoic acid, we found that **5a** was obtained in almost quantitative yield in 30 min at room temperature catalyzed by 1 mol % of $[\text{Cp}^*\text{RhCl}_2]_2$ (Scheme 5, a) without

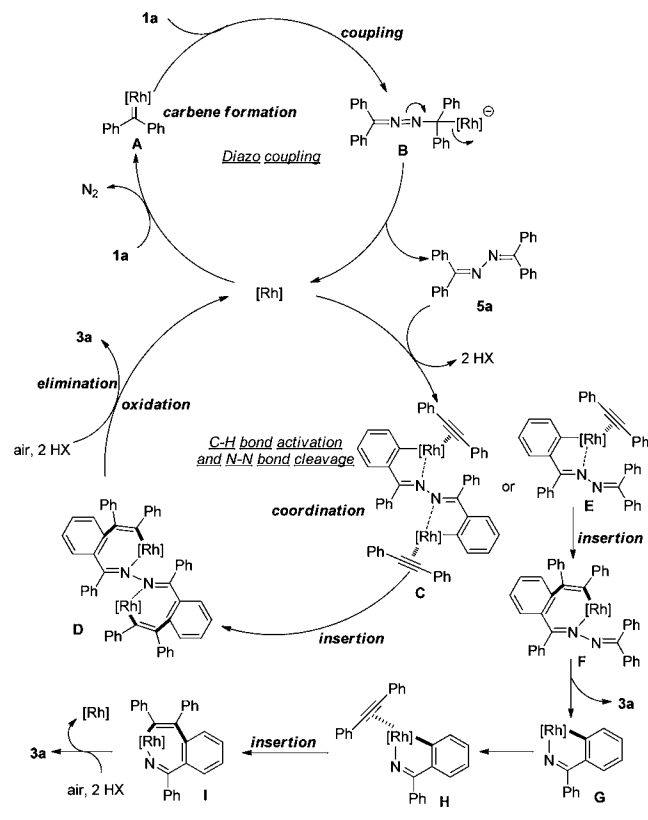
Scheme 5. Control Experiments



the detection of alkene. Next, **5a** was treated under standard reaction conditions (same with Scheme 3), and **3a** was isolated in 90% yield (Scheme 5, b).¹² These results disclosed that the rhodium-catalyzed C–H functionalization of donor/donor diazo compounds is a tandem process.

On the basis of the above experiments, a plausible reaction mechanism is proposed (Scheme 6). The first catalytic cycle is

Scheme 6. Proposed Catalytic Cycle



Rh-catalyzed azine formation via diazo coupling. First, the reaction between **1a** and rhodium catalyst generates metal-carbene intermediate **A**, which rapidly undergoes attack by another molecule of **1a** to afford intermediate **B**. Then intramolecular rearrangement of **B** associated with the loss of rhodium catalyst produces azine **5a**. Next, the reaction of **5a** and rhodium catalyst affords intermediate **C** via C–H bond activation, which followed by insertion of alkyne into the Rh–C bond gives rise to intermediate **D**. Finally, the reductive elimination and N–N bond cleavage of **D** in the presence of air and benzoic acid affords two molecules of **3a** and regenerates the active rhodium catalyst. Alternatively, coordination of **5a** with alkyne generates intermediate **E**.¹² Insertion of alkyne into the Rh–C bond affords intermediate **F**, which undergoes reductive elimination and N–N bond cleavage to release **3a** and an active intermediate **G**. Next, **G** coordinates to another molecule of alkyne followed by insertion to give rise to intermediate **I**. Subsequent oxidation by air in the presence of benzoic acid furnishes **3a** and regenerates the catalyst.

In summary, we have demonstrated an unprecedented rhodium-catalyzed C–H functionalization of aryl diazo compounds. This novel transformation features a tandem process of diazo coupling, C–H bond activation, and N–N bond cleavage in the presence of a single rhodium catalyst. Further, an external co-oxidant such as copper complex, which is commonly used in C–H bond activation, is not needed.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures along with characterizing data and copies of NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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