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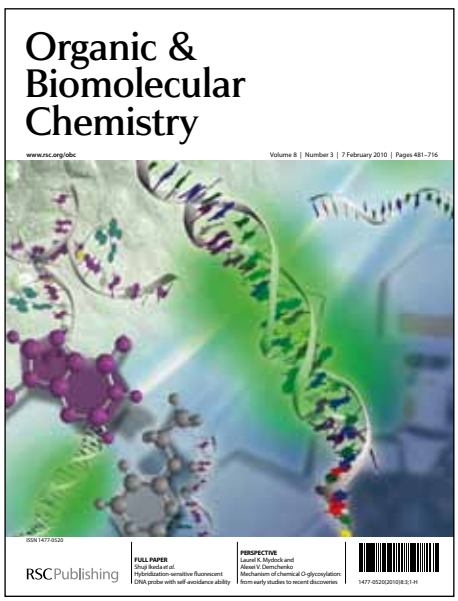

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ARTICLE TYPE

Rhodium-Catalyzed Intermolecular Hydroarylation of Internal Alkynes with *N*-1-Phenylbenzotriazoles

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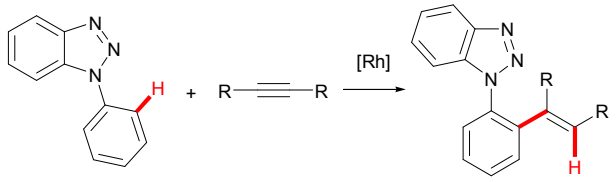
A rhodium-catalyzed intermolecular hydroarylation of internal alkynes with *N*-1-phenylbenzotriazoles via C-H bond activation is described. This transformation offers an alternative method for the hydroarylation of internal alkynes with high stereoselectivity. The reaction mechanism was discussed according to the deuterium-labeling experiments.

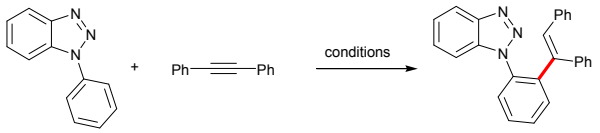
The hydroarylation reaction of alkynes serves as a powerful tool for the construction of styrene derivatives in an atom-efficient manner.[1] Generally, hydroarylation of alkynes occurs by two different mechanisms: 1) hydroarylation by electrophilic aromatic substitution (EAS), in which a cationic metal complex is employed for the activation of alkynes, followed by electrophilic aromatic substitution to deliver the products. However, the scope and utility are limited since the use of electron-rich arenes is indispensable.[2] 2) hydroarylation by C-H activation, in which a directing group is generally required and a broad range of substrates is compatible.[3] Although Ackermann's pioneering works on ruthenium-catalyzed arylation via C-H bond activation using triazolyl as directing group has been reported,[4] as far as we know, there is no report using 1-benzotriazolyl as directing group for the hydroarylation of alkynes. Moreover, regio- or stereoisomeric mixtures are often obtained in traditional methods[2i,3e,5]. Herein, we report a rhodium-catalyzed intermolecular stereoselective hydroarylation of internal alkynes with *N*-1-phenylbenzotriazoles via C-H activation (Scheme 1).



Scheme 1 Intermolecular hydroarylation of internal alkynes with *N*-1-phenylbenzotriazoles

Initially, $RhCl(PPh_3)_3$ was chosen as the catalyst for the intermolecular reaction between benzotriazole **1a** and diphenylacetylene **2a**. However, only a trace of the desired product **3aa** was detected when the reaction was carried out at 160 °C in toluene (Table 1, entry 1). Gratifyingly, the addition of $AgSbF_6$ (5 mol %) could greatly improve the yield (56%, entry 2). The structure of *syn*-addition product was identified by X-ray diffraction. It is worth noting that no product was observed in the absence of rhodium (entry 3) and no *trans*-addition isomer or other products could be detected in the

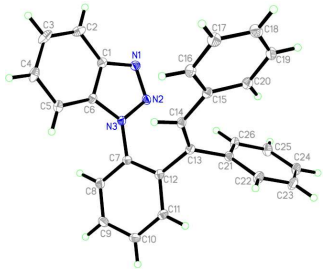
Table 1 Optimization of reaction conditions [a]



1a **2a** **3aa**

Entry	Cat. (mol %)	Additives (mol %)	Solvent	Yield (%)[b]
1	$RhCl(PPh_3)_3$ (2.5)	----	Toluene	trace
2	$RhCl(PPh_3)_3$ (2.5)	$AgSbF_6$ (5.0)	Toluene	56
3	----	$AgSbF_6$ (5.0)	Toluene	0
4	$RhCl(PPh_3)_3$ (2.5)	$AgSbF_6$ (5.0)	1,4-Dioxane	9
5	$RhCl(PPh_3)_3$ (2.5)	$AgSbF_6$ (5.0)	Bu_2O	37
6	$RhCl(PPh_3)_3$ (2.5)	$AgSbF_6$ (5.0)	DCE	24
7	$RhCl(PPh_3)_3$ (2.5)	$AgSbF_6$ (5.0)	DMF	3
8	$RhCl(PPh_3)_3$ (2.5)	$AgSbF_6$ (5.0)	DMSO	4
9	$RhCl(PPh_3)_3$ (2.5)	$AgSbF_6$ (5.0)	PhCl	27
10	$RhCl(PPh_3)_3$ (2.5)	$AgSbF_6$ (5.0)	*p*-Xylene	32
11	$RhCl(PPh_3)_3$ (2.5)	$AgSbF_6$ (5.0)	Mesitylene	88
12[c]	$RhCl(PPh_3)_3$ (2.5)	$AgSbF_6$ (5.0)	Mesitylene	56
13	$Rh(CO)Cl(PPh_3)_2$ (2.5)	$AgSbF_6$ (5.0)	Mesitylene	trace
14	$[RhCl(cod)_2]_2$ (2.5)	$AgSbF_6$ (5.0)	Mesitylene	trace
15	$RhCl(C_8H_{14})_2$ (2.5)	$AgSbF_6$ (5.0)	Mesitylene	trace
16	$RhCl(PPh_3)_3$ (2.5)	AgF (5.0)	Mesitylene	8
17	$RhCl(PPh_3)_3$ (2.5)	$AgBF_4$ (5.0)	Mesitylene	trace
18	$RhCl(PPh_3)_3$ (2.5)	$AgOCOCF_3$ (5.0)	Mesitylene	11
19	$RhCl(PPh_3)_3$ (2.5)	AgOTf (5.0)	Mesitylene	96
20	$RhCl(PPh_3)_3$ (1.5)	AgOTf (5.0)	Mesitylene	15
21	$RhCl(PPh_3)_3$ (2.5)	AgOTf (2.5)	Mesitylene	72
22[d]	$RhCl(PPh_3)_3$ (2.5)	AgOTf (5.0)	Mesitylene	67
23[e]	**$RhCl(PPh_3)_3$ (2.5)**	**AgOTf (5.0)**	**Mesitylene**	**98**
24[e,f]	$RhCl(PPh_3)_3$ (2.5)	AgOTf (5.0)	Mesitylene	0

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst, additive and solvent (1.6 mL) at 160 °C in seal tube under N_2 for 20 h. [b] Isolated yield. [c] 140 °C. [d] 0.2 mmol of **2a** was used. [e] 12 h. [f] The reaction was carried out under air.



ORTEP drawing of **3aa**

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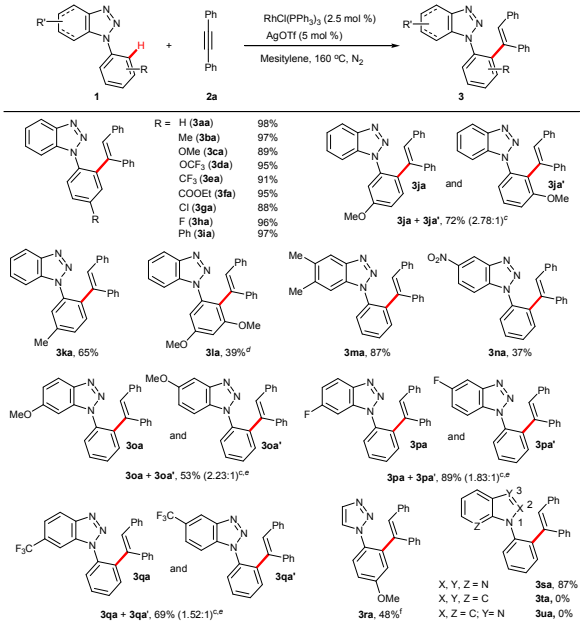
reaction mixture. Carrying out the reaction in other solvents, such as 1,4-dioxane, Bu_2O, DCE, DMF, DMSO, PhCl and *p*-xylene did not result in any improvement in yield until mesitylene was chosen (entries 4-11), and lower temperature led to lower yield (entry 12). Moreover, treatment of **1a** and **2a** with other rhodium catalysts could not afford **3aa** in comparable yield (entries 13-15). On the contrary, the addition of AgOTf led the yield to a high level (entry 19). Lower catalyst and silver salt loading or **2a** dosage decreased the yield noticeably (entries 20-22). Finally, the yield was improved slightly by a shortened reaction time (entry 23). No appreciable reaction was observed when the reaction was carried out under air, indicating that oxygen retards the reaction significantly (entry 24)

On the basis of above observations, the substrate scope was explored subsequently. The effect of different substituents on benzotriazole **1** is summarized in Table 2. Under the optimized reaction conditions, electron-donating functional groups, such as methyl, methoxy, trifluoromethoxy, electro-withdrawing functional groups, such as trifluoromethyl and ethoxy carbonyl, halo substituents, such as chloro and fluoro, or phenyl on N-aryl moiety were well-tolerated, delivering the corresponding products **3ba** - **3ia** in good to excellent yields. It is worth noting that substrate with *meta*-methoxy substituent led to the product as mixtures with the ratio of 2.78:1 (**3ja**/**3ja'**), while substrate with *meta*-methyl substituent afforded the product **3ka** exclusively, and the steric hinderance affected the yield tremendously (**3la**).

Table 2. The reaction of diphenylacetylene (**2a**) with various 1-phenyl-1H-benzo[1,2,3]triazole [a,b]

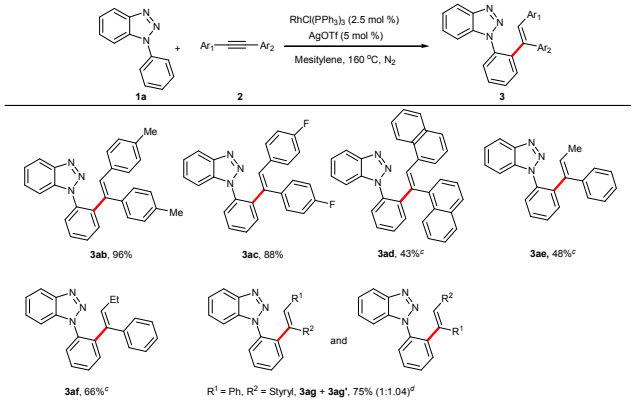


[a] Reaction conditions: **1** (0.2 mmol), **2a** (0.3 mmol), $RhCl(PPh_3)_3$ (2.5 mol %), AgOTf (5.0 mol %), mesitylene (1.6 mL) at 160 °C for 12 h under N_2. [b] Isolated yield. [c] Determined by ^1H NMR. [d] $RhCl(PPh_3)_3$ (5.0 mol %) and AgOTf (10.0 mol %) were used. [e] A mixture of benzotriazole **1** was used, see ref. 6 for details. [f] 50 h.

On the other hand, substrates with different substituents on the benzotriazolyl moiety were also examined. Substrates with methyl and nitro were tolerated (**3ma** and **3na**). Notably, a mixture of benzotriazoles could be smoothly converted to the desired products in moderate to good yields.[6] Moreover, the reaction afforded **3ra** and **3sa** in acceptable yields but none of product **3ta** or **3ua**, indicating that the existence of *N*-2 atom on benzotriazolyl moiety is crucial for the transformation.

The data of different acetylenes reacting with benzotriazole **1a** is listed in Table 3. Diphenyl acetylene with substituents, such as methyl and fluoro, and dinaphthalenyl acetylene could be transformed into the desired products in moderate to excellent yields (**3ab**, **3ac** and **3ad**). In addition, although the reaction gave the target products as mixtures when phenylstyryl acetylene was used (**3ag** and **3ag'**), a single isomer was detected when alkylphenyl acetylenes were employed (**3ae** and **3af**).

Table 3. The reaction of different acetylene with 1-phenyl-1H-benzo[1,2,3]triazole (**1a**) [a,b]



[a] Reaction conditions: substrate **1a** (0.2 mmol), **2** (0.3 mmol), $RhCl(PPh_3)_3$ (2.5 mol %), AgOTf (5.0 mol %), mesitylene (1.6 mL) at 160 °C under N_2 for 12 h. [b] Isolated yield. [c] $RhCl(PPh_3)_3$ (5.0 mol %) and AgOTf (10.0 mol %) were used. [d] Determined by ^1H NMR.

To probe the reaction mechanism, deuterium-labeling experiments were conducted. First of all, treatment of deuterated benzotriazole **1a**-d_5 with the optimized conditions led to a deuterium incorporation in the olefinic position of the product, indicating that an oxidative addition of the *ortho* C-H bond is possible (Scheme 2, a). The high selectivity for *syn*-insertion renders the possibility of alkyne activation improbable. Secondly, there is no appreciable deuterium loss at the *ortho* position of product **3aa**-d_5 as well as recovered **1a**-d_5, implying that the oxidative addition of the *ortho* C-H is irreversible. Then, intermolecular kinetic isotope effects (k_H/k_D = 1.67) indicates that C-H activation is not involved in the rate-limiting step (Scheme 2, b). Finally, intramolecular kinetic isotope effects (k_H/k_D = 2.1) implys that the reaction occurs by a C-H activation mechanism (Scheme 2, c).

On the basis of these primary results, a possible catalytic cycle is proposed and illustrated in Scheme 3. Initially, $RhCl(PPh_3)_3$ reacts with AgOTf to generate the active rhodium species. The catalytic cycle is initiated by the

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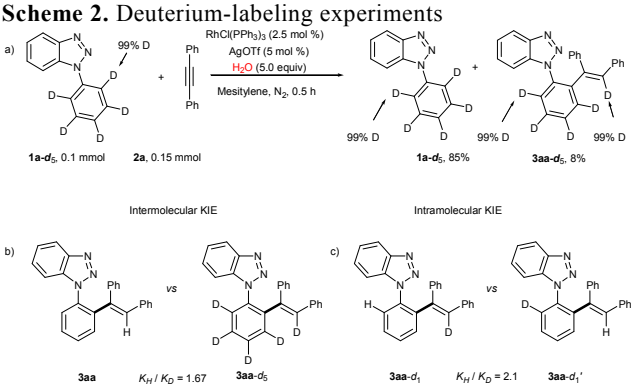
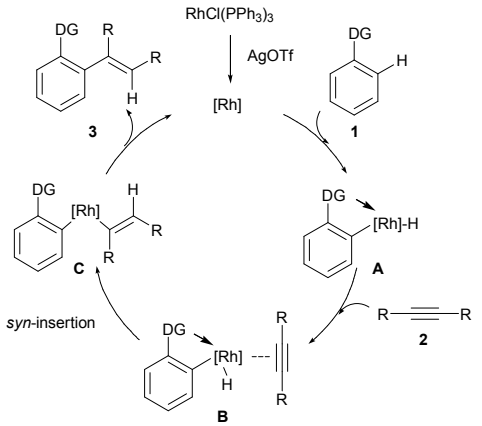
Scheme 2. Deuterium-labeling experiments



formation of σ-arylrhodium intermediate **A** by a chelation-assisted oxidative additon of the *ortho* C-H bond, followed by coordination with alkyne **2** to form complex **B**. Then, *syn*-insertion into the alkyne gives transient intermediate **C**. At last, reductive elimination delivers the product and releases the catalytic species.[7]

Scheme 3. Proposed catalytic cycle



In conclusion, we have demonstrated a rhodium-catalyzed intermolecular hydroarylation of internal alkynes via C-H bond activation. This reaction provides an alternative method for the hydroarylation of internal alkynes with high stereoselectivity. The mechanism was discussed according to the isotope labeling experiments. Further studies on the hydroarylation of alkyne are under investigation in our group.

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† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

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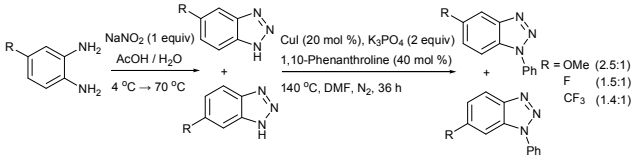
6 a mixture of *N*-aryl benzotriazoles was obatined when we try to synthesize them according to the reported methods and used as substrate directly. Their ratios were determined by GC.



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