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Rhodium-Catalyzed Oxidative Benzannulation of *N*-Adamantyl-1-naphthylamines with Internal Alkynes via Dual C−H Bond Activation: Synthesis of Substituted Anthracenes

Xuan Zhang,[†,∥] Xiaoqiang Yu,[*,†] Dingwei Ji,[†] Yoshinori Yamamoto,[†,‡] Abdulrahman I. Almansour,[§] Natarajan Arumugam,[§] Raju Suresh Kumar,[§] and Ming Bao[*,†]

[†]State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian 116023, China

[‡]WPI-AIMR (WPI-Advanced Institute for Materials Research), Tohoku University, Sendai 980-8577, Japan

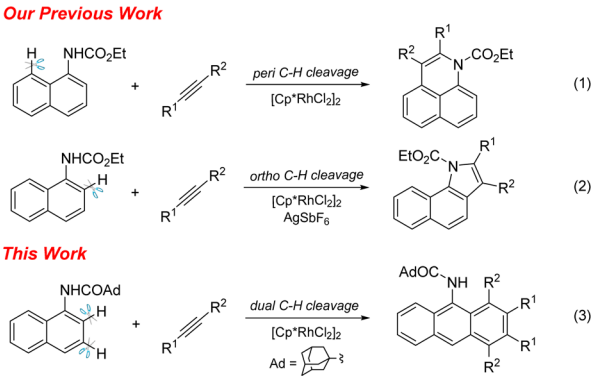
[§]Department of Chemistry, College of Sciences, King Saud University, P.O. Box 2455, Riyadh 11451, Saudi Arabia

Supporting Information

ABSTRACT: Rhodium-catalyzed oxidative benzannulation of *N*-adamantyl-1-naphthylamines with internal alkynes to produce highly substituted anthracenes in satisfactory to good yields was developed. The annulation reaction proceeded smoothly under mild conditions in the presence of $[Cp^*RhCl_2]_2$ as the precatalyst and $Cu(OAc)_2$ as the oxidant.

The development of convenient and efficient methods for the synthesis of polycyclic aromatic compounds has attracted considerable attention. Polycyclic aromatic compounds can be utilized as versatile and key synthetic intermediates for the preparation of organic semiconductors and luminescent materials.[1] Numerous methods, including the Diels−Alder reaction of benzynes with cyclopentadienones,[2] aromatic homologation of organometallic reagents with alkynes,[3] and transition-metal-catalyzed aromatic homologation of appropriate aromatic substrates with alkynes,[4] have been developed over the past years. Transition-metal-catalyzed aromatic homologation is the most economical and practical among these methods. In particular, this type of aromatic homologation that proceeds through double C−H bond cleavage has been used as extremely powerful tools for the synthesis of highly substituted polycyclic aromatic compounds. The above-mentioned synthetic method usually requires a suitable directing group linked on the aromatic substrate. Heterocycles (such as pyrazole,[4j] benzoimidazole,[4t] and pyridine[4d]), aminocarbonyl groups,[4h,i] and acetylamino groups[4n,r] have been employed as effective directing groups for this purpose. An acylamino group could be easily installed into aromatic substrates and converted to other functional groups. Thus, acylamino groups were frequently utilized as directing groups for C−H bond activation.[5]

We have recently found that reaction regioselectivity in the oxidative annulation of ethyl naphthalen-1-ylcarbamates with internal alkynes could be easily controlled by using different rhodium catalyst systems.[6] The benzoquinoline formation reaction proceeded via *peri*-C−H bond cleavage in the presence of a neutral rhodium catalyst (eq 1), whereas the benzoindole formation reaction proceeded via *ortho*-C−H bond cleavage in the presence of a cationic rhodium catalyst (eq 2). During the continuing research on the rhodium-catalyzed C−H bond activation of naphthalene substrates with acylamino directing groups, we succeeded in the benzannulation by using a sterically hindered directing group (adamantoylamino) for the first time (eq 3).[7] The results are reported in the current work.



In the initial study, we examined the reaction of *N*-(naphthalen-1-yl)acetamide (**1a**) with 1,2-diphenylethyne (**4a**) in the presence of $[Cp^*RhCl_2]_2$ as the precatalyst and $Cu(OAc)_2$ as the oxidant in *N*,*N*-dimethylformamide (DMF) at 110 °C for 12 h. A similar result was observed as reported by Fagnou and co-workers.[4r] Benzoindole formation reaction exclusively occurred via *ortho*-C−H bond cleavage to produce **5a′** in 21% yield (Scheme 1). We then considered that a sterically hindered directing group may inhibit the occurrence of an undesired benzoindole forming reaction to take place. The undesired reaction was completely inhibited when the methyl in the *N*-acyl group was replaced with *tert*-butyl. The benzannulation product **6a** was isolated in 39% yield (Scheme

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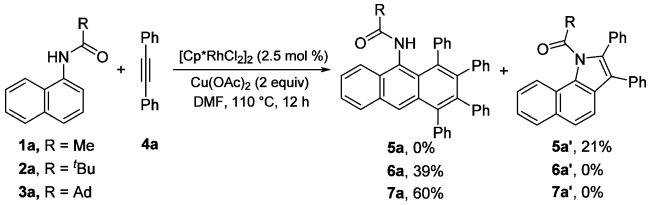
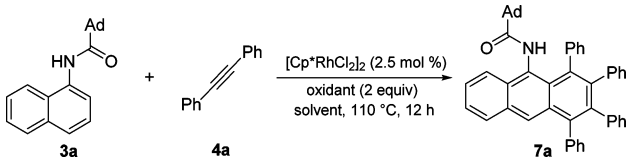
Scheme 1. Effect of Steric Hindrance of Directing Group on Reaction Regioselectivity



1). The yield of the benzannulation product could be further improved by installing the more sterically hindered adamantan-1-yl into *N*-acyl group (Scheme 1, **7a**: 60%). Based on these findings, benzannulation reaction conditions were subsequently optimized.

The benzannulation reaction of 1-adamantoyl-1-naphthylamine (**3a**) with **4a** was selected as a model to optimize the reaction conditions. Results are shown in Table 1. The use of

Table 1. Optimization of Reaction Conditions[a]



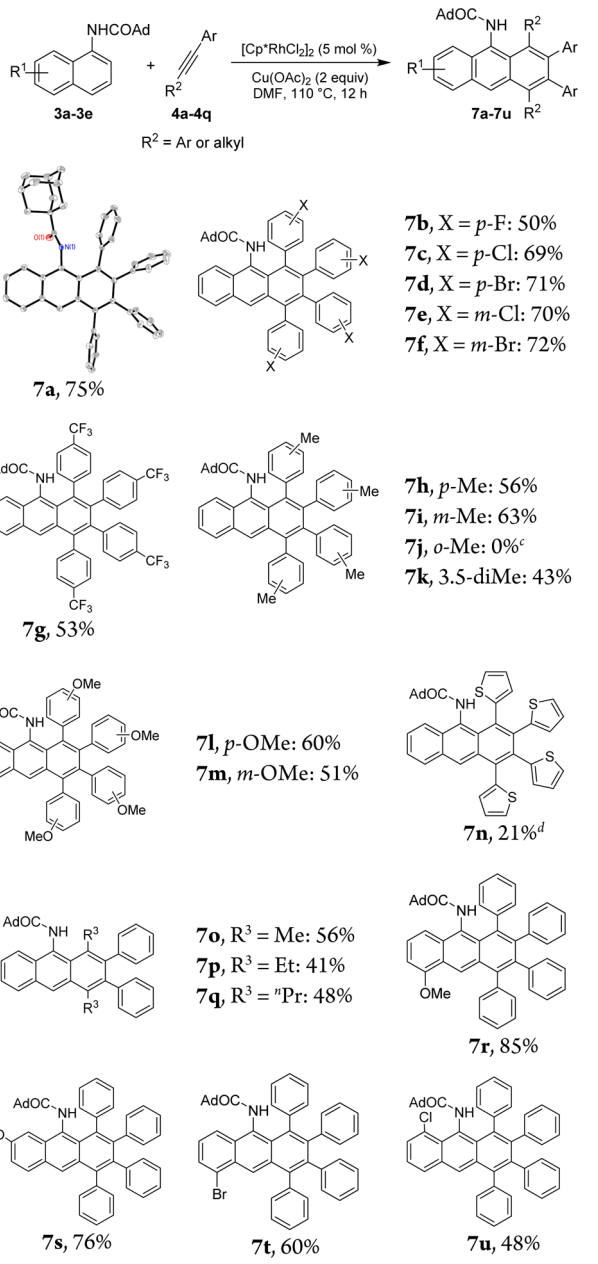
entry	catalyst	oxidant	solvent	yield (%)[b]
1	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2$	DMF	60
2	$RhCl_3·3H_2O$	$Cu(OAc)_2$	DMF	NR[c]
3	$RhCl(PPh_3)_3$	$Cu(OAc)_2$	DMF	NR[c]
4	$[Ru(p\text{-cymene})Cl_2]_2$	$Cu(OAc)_2$	DMF	NR[c]
5	$Pd(OAc)_2$	$Cu(OAc)_2$	DMF	NR[c]
6	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2$	toluene	21
7	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2$	dioxane	33
8	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2$	acetone	55
9	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2$	DCE	40
10	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2$	^{t}AmOH	32
11[d]	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2$	DMF	71
12[d,e]	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2$	DMF	75
13[d,e]	$[Cp^*RhCl_2]_2$	$Cu(OTf)_2$	DMF	NR[c]
14[d,e]	$[Cp^*RhCl_2]_2$	Ag_2CO_3	DMF	NR[c]
15[d,e]	$[Cp^*RhCl_2]_2$	AgOAc	DMF	trace

[a]Reaction conditions: **3a** (0.25 mmol), **4a** (0.5 mmol), catalyst (2.5 mol %), oxidant (0.5 mmol) in solvent (2.0 mL) at 110 °C for 12 h under a N_2 atmosphere. [b]Isolated yield. [c]No reaction was observed, and the starting materials were recovered. [d]5.0 mol % of $[Cp^*RhCl_2]_2$ was used. [e]0.75 mmol of **4a** was used.

$RhCl_3·3H_2O$ and $RhCl(PPh_3)_3$ as rhodium precatalysts instead of $[Cp^*RhCl_2]_2$ led to no reaction (entries 2 and 3). Dichloro(*p*-cymene)ruthenium dimer $\{[Ru(p\text{-cymene})Cl_2]_2\}$ and $Pd(OAc)_2$ were demonstrated to be also totally ineffective (entries 4 and 5). The solvents were then screened using nonpolar [toluene and 1,2-dichloroethane (DCE)] and polar [DMF, dioxane, acetone, and *tert*-amyl alcohol (^{t}AmOH)] solvents (entries 1 and 6–10). DMF proved to be the best solvent (entry 1). The yield of benzannulation product **7a** was found to increase with increased $[Cp^*RhCl_2]_2$ loading (entry 11, 71%). The yield of **7a** was found to be further increased when the amount of **4a** was increased to 3.0 equiv (entry 12, 75%). The oxidants, including $Cu(OAc)_2$, $Cu(OTf)_2$, Ag_2CO_3, and AgOAc, were finally screened using $[Cp^*RhCl_2]_2$ as the precatalyst and DMF as the solvent. Among the tested oxidants, the $Cu(OAc)_2$ proved to be the best oxidant (entry 12 versus entries 13–15). Therefore, the subsequent benzannulation reactions of 1-adamantoyl-1-naphthylamines **3a–3e** with internal alkynes **4a–4q** were performed in the presence of $[Cp^*RhCl_2]_2$ as the precatalyst and $Cu(OAc)_2$ as the oxidant in DMF at 110 °C for 12 h.

With the optimized reaction conditions in hand, we explored the scope and the limitation of this type of benzannulation, and the results are summarized in Scheme 2. As described in Table 1, the desired product **7a** was obtained in 75% yield. Reactions

Scheme 2. Rh(III)-Catalyzed Oxidative Benzannulation of 1-Adamantoyl-1-naphthylamines with Internal Alkynes[a,b]



[a]Reaction conditions: **3** (0.25 mmol), **4** (0.75 mmol), $[Cp^*RhCl_2]_2$ (5 mol %, 7.8 mg), $Cu(OAc)_2$ (0.5 mmol, 91.0 mg) in DMF (2.0 mL) at 110 °C for 12 h under N_2 atm. [b]Isolated yields. [c]No reaction; starting materials were recovered. [d]10 mol % of $[Cp^*RhCl_2]_2$ was used.

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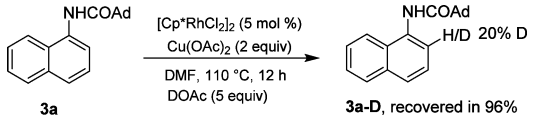
of **3a** with internal alkynes **4b**−**4f** bearing halogen atoms on *para*- or *meta*-positions of the benzene rings proceeded smoothly to produce the corresponding benzannulation products **7b**−**7f** in satisfactory yields (50%−72%). The reaction of **3a** with internal alkynes **4g** bearing an electron-withdrawing group CF_3 on the *para*-positions of the benzene rings provided the benzannulation product **7g** in 53% yield. Internal alkynes **4h**−**4m** bearing an electron-donating group methyl (Me) or methoxy (OMe) on benzene rings were subsequently examined, and the corresponding benzannulation products **7h**, **7i**, and **7k**−**7m** were obtained in moderate-to-satisfactory yields (43%−63%), except **7j**. The reason for the nonreaction observed in the treatment of **3a** with **4j** may be due to steric hindrance caused by the *ortho*-methyl group in **4j**. These results mentioned above indicate that the electron property of the substituent linked on the benzene rings of alkynes did not influence alkyne reactivity. The applicability of an internal alkyne with a heterocycle such as thiophene was also investigated, and 21% of benzannulation product **7n** was obtained. Surprisingly, the use of unsymmetrical alkynes **4o**−**4q**, which bear a phenyl group and an alkyl group (Me, Et, and ^{n}Pr), led to the formation of **7o**−**7q** as sole products, respectively (41%−56% yields).[8] The reactivities of 1-adamantoyl-1-naphthylamines **3b**−**3e**, with MeO, Br, and Cl on the naphthalene ring, respectively, were finally investigated by using **4a** as a reaction partner. The corresponding benzannulation products **7r**−**7u** were obtained in moderate-to-good yields (48%−85%). All new products, **7a**−**7i** and **7k**−**7u**, were identified through their NMR and HRMS data, as well as IR spectra. Product **7a** was further identified by determining its X-ray structure.[9]

To elucidate the mechanism of this type of benzannulation reaction, we conducted a H−D exchange experiment to investigate whether these reactions initially proceeded via an *ortho*-C−H bond cleavage pathway (Scheme 3). We found that

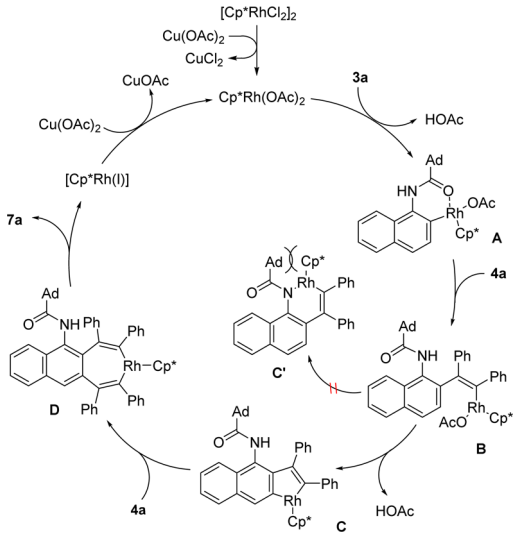
Scheme 3. H−D Exchange Experiment on Amide Substrate 3a in the Presence of DOAc



20% of *ortho*-H in **3a** was replaced by D. This result reveals that metalation is directed by the amide group and that cyclorhodation is a reversible process in the absence of an alkyne under the protonic conditions.

On the basis of our experimental outcomes and previous reports,[4h−j] a plausible catalytic cycle is proposed to account for the present catalytic benzannulation reaction (Scheme 4). The catalytic cycle starts from $Cp^*Rh(OAc)_2$, which is generated in situ from the ligand exchange reaction between $[Cp^*RhCl_2]_2$ and $Cu(OAc)_2$. Coordination of the oxygen atom of **3a** to the rhodium catalyst species and subsequent *ortho* C−H bond activation would generate a six-membered rhodacyclic intermediate **A** with the liberation of an acetic acid molecule. Then, the insertion of internal alkyne **4a** into the Rh−C bond would occur to produce intermediate **B**, which would subsequently undergo a second C−H bond activation to afford intermediate **C**. A second insertion of alkyne **4a** and subsequent reductive elimination would occur to generate highly substituted anthracene product **7a** and a Rh(I) species. The Rh(I) species

Scheme 4. A Plausible Mechanism for the Rh-Catalyzed Benzannulation



would then be reoxidized to active catalytic species $Cp^*Rh(OAc)_2$ by $Cu(OAc)_2$. The formation of intermediate **C′** is considered to be inhibited by the steric hindrance of the adamantan-1-yl group. Consequently, the formation of the benzoindole product was inhibited.

In summary, we developed a rhodium-catalyzed regioselective oxidative benzannulation by using a sterically hindered adamantoylamino group as the directing group for the synthesis of highly substituted anthracenes. A series of highly substituted anthracenes were obtained in moderate-to-high yields from the reactions of 1-adamantoyl-1-naphthylamines with internal alkynes via dual C−H bond cleavages. To the best of our knowledge, this paper presents the first successful example of the rhodium-catalyzed benzannulation of *N*-acyl 1-naphthylamines.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01991.

Experimental procedures and characterization data (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: yuxiaoqiang@dlut.edu.cn.
*E-mail: mingbao@dlut.edu.cn.

Present Address

[‖]Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523, United States.

Notes

The authors declare no competing financial interest.

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(7) Only a trace amount of benzannulation product was observed when a palladium catalyst was used under literature conditions (see 4n).

(8) The structure of **7o** was surmised according to the nuclear Overhauser effect (NOE) determination and the literature. (a) See 4j. (b) See 4t. (c) Kim, Y.; Hong, S. *Chem. Commun.* **2015**, *51*, 11202.

(9) The structure of **7a** was confirmed by X-ray single crystal diffraction analysis. For details, see the Supporting Information.

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