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Synthesis of Conjugated Polycyclic Quinoliniums by Rhodium(III)-Catalyzed Multiple C−H Activation and Annulation of Arylpyridiniums with Alkynes

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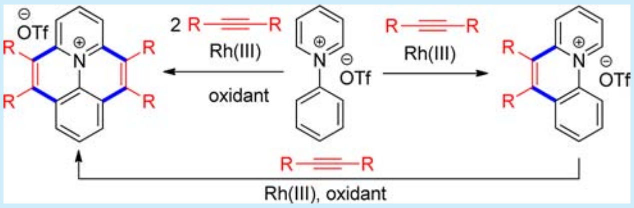
S *Supporting Information*

ABSTRACT: A simple method for the efficient synthesis of highly substituted pyrido[1,2-*a*]quinolinium- and quinolizino-[3,4,5,6-*ija*]quinolinium-based polyheteroaromatic compounds via rhodium(III)-catalyzed multiple C−H activation annulation reactions has been developed. Moreover, some of the quinolizino[3,4,5,6-*ija*]quinolinium salts exhibit intense fluorescence and have potential application in optoelectronic materials.



Transition-metal-catalyzed aromatic C−H bond activation represents a promising strategy for the construction of various aromatic or heteroaromatic molecules because of its high efficiency, step and atom economy, and functional group tolerance.[1,2] Fused polycyclic aromatic and polycyclic heteroaromatic compounds are embedded in a large number of compounds because of their potential utility in organic and polymeric functional materials.[3] Therefore, the synthesis of such π-conjugated systems is highly desirable. Recently, the synthesis of polycyclic π-conjugated aromatics and heteroaromatics via Rh(III)-catalyzed double/multiple C−H activation between arenes/heteroarenes and alkynes have been extensively investigated.[4−6] Several research groups have reported the synthesis of polycyclic aromatic/heteroaromatic compounds by Rh(III)-catalyzed double/multiple C−H bond activation with heteroatom-assisted chelation.[4] The group of Choudhury and our group reported the synthesis of imidazoquinolinium salts through Rh(III)-catalyzed double/multiple C−H bond activation with the assistance of N-heterocyclic carbenes (NHCs) as directing groups.[5] Miura and Satoh, Chen, Cramer, and our group reported the synthesis of naphthothiophene, polycyclic quinolines, and extended arenes via direct double C−H activation without chelation assistance (Scheme 1a).[6]

Encouraged by such results and following our continuous interest in Rh(III)-catalyzed C−H bond activation and heterocycle building,[4f,5e,6f,7] herein we report an efficient Rh(III)-catalyzed reaction of arylpyridiniums with alkynes to afford pyrido[1,2-*a*]quinolinium salts and quinolizino[3,4,5,6-*ija*]quinolinium salts (Scheme 1b). Extended quinolinium salts, expressing appealing electrochemical features and electronic and photophysical properties, are among the most valuable backbones and have potential applications in dyes, electronic and optoelectronic devices, and nonlinear optical materials.[8]

In an initial attempt, the reaction of 1-phenylpyridinium trifluoromethanesulfonate (**1a**) with diphenylacetylene (**2a**) was explored to screen the reaction conditions (Table 1). **1a** (0.2 mmol) was treated with **2a** (0.24 mmol) in the presence of $[Cp^*RhCl_2]_2$ (0.01 mmol) and $Cu(OAc)_2 \cdot H_2O$ (0.4 mmol) in CH_3CN at 80 °C for 12 h under an Ar atomosphere, and the desired product **3aa** was obtained in 23% yield (entry 1). The structure of compound **3aa** was confirmed by ^1H, ^{13}C, and ^{19}F NMR spectroscopy and high-resolution mass spectrometry (HRMS). Switching the oxidant to AgOAc and $Cu(OAc)_2$ afforded the desired product **3aa** in 29% and 62% yield, respectively (entries 2 and 3). In the absence of catalyst or oxidant, **3aa** was not formed. The choice of solvent was crucial for the efficiency of this process. CH_3CN was found to be the ideal solvent (Table S1 in the Supporting Information (SI)). When the reaction time was increased to 20 h, the reaction yield rose to 78% (entry 5). Pleasingly, when the amount of **1a** was changed to 0.22 mmol and the temperature was increased to 100 °C, the yield increased to 93% (entry 8). Lower oxidant loading resulted in a lower yield of **3aa** (entry 9).

With the optimal reaction conditions established, we first examined the reactions of variously substituted 1-phenylpyridinium trifluoromethanesulfonates **1b−i** with **2a** (Scheme 2). 4-Methyl and 4-*tert*-butyl substituents on the phenyl ring as well as 4-methyl and 4-phenyl substituents on the pyridyl ring were tolerated under the standard conditions to afford **3da−ea** and **3ga−ha** in good yields (81−94%). 4-Fluoro- and 4-

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Scheme 1. Rh(III)-Catalyzed Oxidative Annulation with Alkynes via C−H Activation

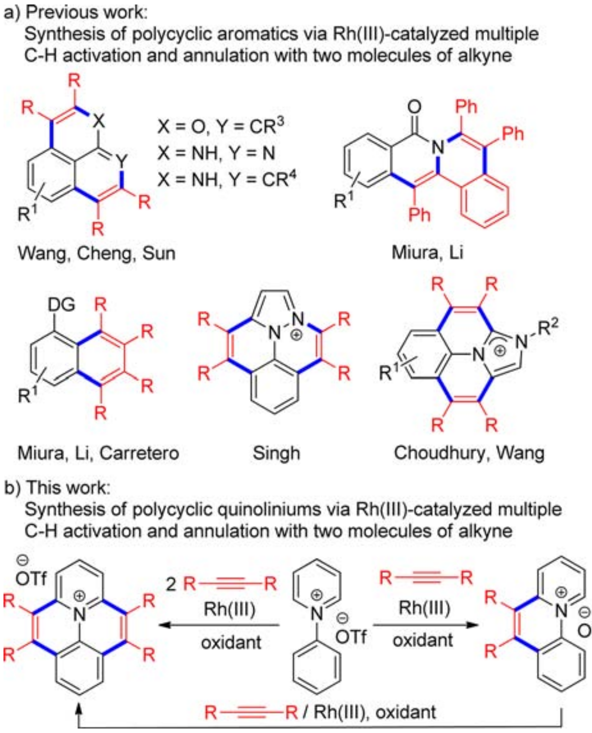
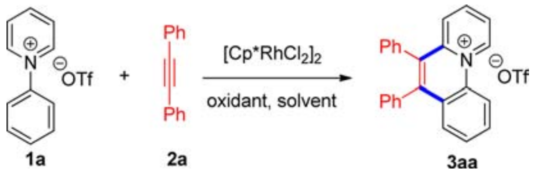


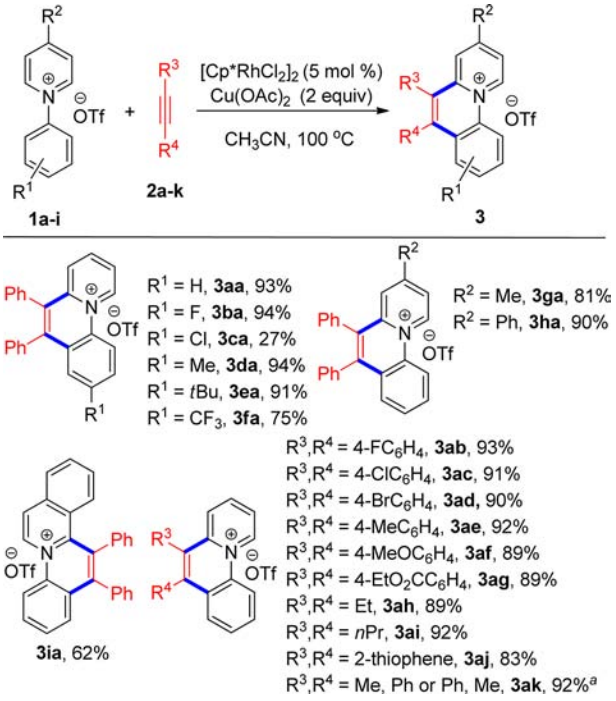
Table 1. Optimization of the Reaction Conditions for the Synthesis of Salt 3aa[a]



entry	oxidant (equiv)	mmol of 2a	yield (%)[b]
1	Cu(OAc)$_2$·H$_2$O (2)	0.24	23
2	AgOAc (2)	0.24	29
3	Cu(OAc)$_2$ (2)	0.24	62
4	–	0.24	0
5[c]	Cu(OAc)$_2$ (2)	0.24	78
6[d]	Cu(OAc)$_2$ (2)	0.24	79
7[d]	Cu(OAc)$_2$ (2)	0.2	90
8[d,e]	Cu(OAc)$_2$ (2)	0.2	93
9[d,e]	Cu(OAc)$_2$ (1)	0.2	80

[a] Reaction conditions: **1a** (0.2 mmol), [Cp*RhCl$_2$]$_2$ (5 mol %), oxidant (0.4 mmol), CH$_3$CN (2.0 mL), 80 °C, Ar atmosphere, 12 h. [b] Isolated yields. [c] Reaction time 20 h. [d] 100 °C. [e] **1a** (0.22 mmol).

Scheme 2. Substrate Scope of Rhodium-Catalyzed 1:1 Oxidative Annulation with Alkynes



[a] A mixture of two regioisomers of **3ak** was obtained in 92% combined yield in a ratio of 4:1.

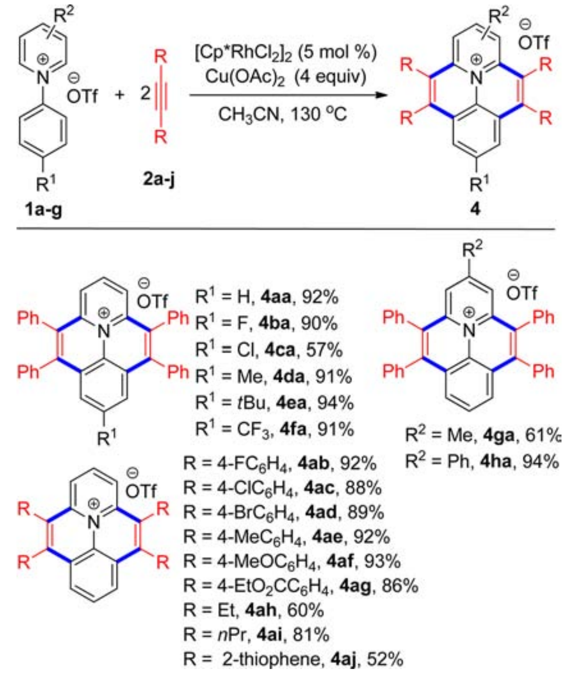
trifluoromethyl-substituted phenylpyridinium salts **1b** and **1f** reacted with **2a** to give **3ba** and **3fa**, respectively, in excellent yields. However, 4-chlorophenylpyridinium salt **1c** provided **3ca** in only 27% yield and produced other uncertain byproducts. This probably occurred because the pyridinium cation is a strong electron-withdrawing group that activated the C−Cl bond. Aside from **2a**, other symmetrical alkynes were also tested for the present reaction (Scheme 2). Both diarylacetylenes and dialkylacetylenes **2b−i** reacted with **1a** to afford the corresponding products **3ab−ai** in good yields (89−93%). Interestingly, bis(2-thienyl)acetylene (**2j**) also reacted smoothly with **1a** to give the annulated product **3aj** in 83% yield. On the other hand, unsymmetrical alkynes such as 1-phenyl-1-propyne produced two regioisomeric products that could not be separated by column chromatography.

In addition, when the amounts of **2a** and Cu(OAc)$_2$ were increased, **1a** underwent a Rh(III)-catalyzed multiple C−H activation annulation reaction with two molecule of **2a** in CH$_3$CN at 130 °C for 12 h, leading to 4,5,9,10-tetraphenylquinolizino[3,4,5,6-*ija*]quinolinium trifluoromethanesulfonate (**4aa**) (Table S2). The structure of **4aa** was confirmed by ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy, HRMS, and single-crystal X-ray diffraction analysis (Figure S2). As shown in Scheme 3, the couplings of substituted phenylpyridinium salts **1b**, **1d−f**, and **1h** with **2a** took place effectively to afford **4ba**, **4da−fa**, and **4ha** in high yields (90−94%), while 1-(4-chlorophenyl)pyridinium salt (**1c**) and 4-methyl-1-phenylpyridinium salt (**1g**) underwent the coupling with **2a** to produce the corresponding salts **4ca** and **4ga** in moderate yields (57% and 61%), respectively. The alkyne substrates **2b−j** also smoothly completed the reaction in moderate to high yields (52−93%).

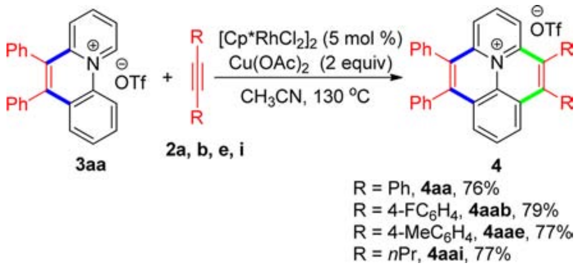
Moreover, **3aa** was used as a substrate for the reactions with alkynes (Scheme 4). Treatment of **3aa** (0.2 mmol) with various alkynes **2** (0.22 mmol) in the presence of [Cp*RhCl$_2$]$_2$ (0.01 mmol) and Cu(OAc)$_2$ (0.4 mmol) in CH$_3$CN at 130 °C for 12 h under an Ar atmosphere gave the corresponding products **4** in good yields (77−79%). When the second alkyne was different from **2a**, such as 1,2-di-*p*-tolylacetylene, 1,2-bis(4-fluorophenyl)acetylene, and 4-octyne, the related annulation products **4aab**, **4aae**, and **4aai** with two different alkynes were obtained.

Furthermore, several experiments were performed to investigate the reaction mechanism. An H/D exchange study

Scheme 3. Substrate Scope of Rhodium-Catalyzed 1:2 Oxidative Annulation with Alkynes



Scheme 4. Reactions of 3aa with Alkynes

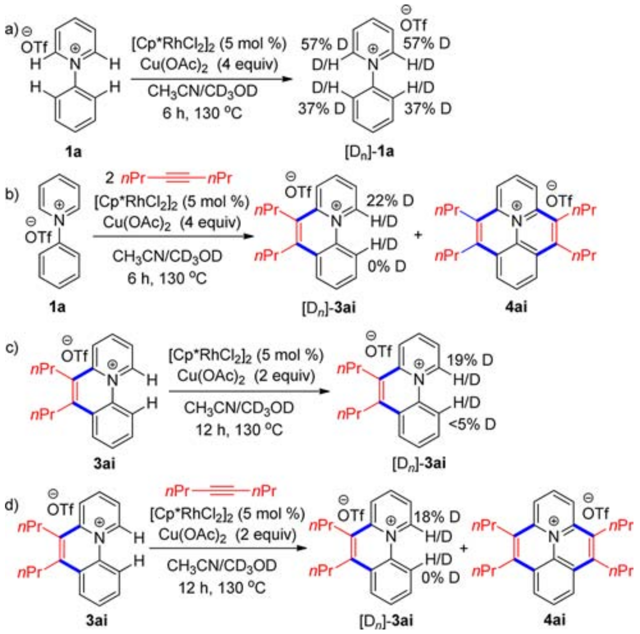


was conducted to examine the nature of the C−H bond activation in the reaction (Scheme 5). When the reactions were performed in the absence of **2i** (Scheme 5a,c), the C_{phenyl}−H and $C_{pyridyl}$−H bonds of **1a** or **3ai** were deuterated. In the presence of **2i**, no deuteration of the C_{phenyl}−H bonds was detected, and the $C_{pyridyl}$−H bond of **3ai** was deuterated (Scheme 5b,d). The results indicate that the reversibility of the C_{phenyl}−H bond activation is altered by addition of 4-octyne while the $C_{pyridyl}$−H bond activation is reversible. Deuterium kinetic isotope effect experiments were also carried out (see the SI). The k_H/k_D value of ∼1.0 for both the reactions affording product **3** and the reactions producing product **4** may suggest that cleavage of the C−H bond of the phenyl ring is not involved in the rate-determining step.

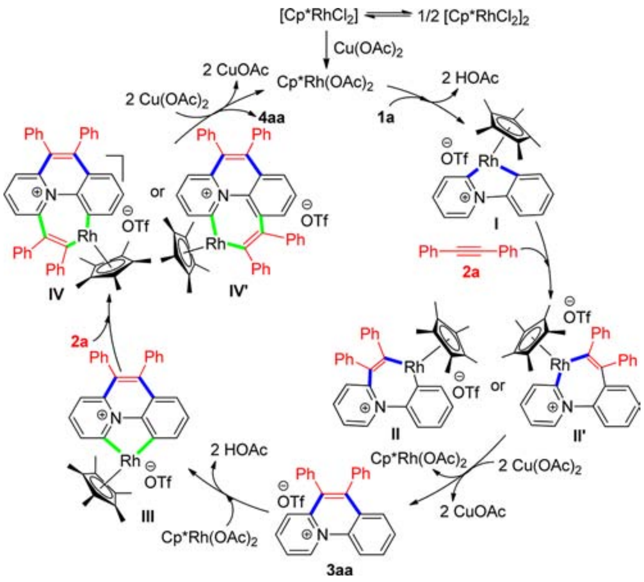
On the basis of the above experimental investigation and related references,[5,9] a possible mechanism is proposed for the present catalytic reaction (Scheme 6). The initial step is likely to be an ortho C−H bond activation directed by the coordinated pyridine-based carbene ligand, thus affording five-membered cyclometalated intermediate **I** by elimination of HOAc. Although we tried and failed to isolate intermediate **I**, there are some reports about the formation of pyridine-based N-heterocyclic carbene metal complexes by reactions of pyridinium with metal complexes.[9] Next, an alkyne coordinates and inserts into the Rh−C bond to give seven-membered rhodacycle **II** or **II′**. Subsequently, reductive elimination of **II** or **II′** results in **3aa** and the rhodium(I) species, which is oxidized to the rhodium(III) species by $Cu(OAc)_2$. Compound **3aa** continuously proceeds with ortho C−H bond activation to afford cyclometalated intermediate **III**. Similar to **I**, an alkyne coordinates and inserts into the Rh−C bond to give seven-membered-ring intermediate **IV** or **IV′**, which subsequently undergoes reductive elimination to afford the annulation product **4aa** and regenerate the rhodium(III) species to continue the catalytic cycle.

To further understand the physical properties of these products, we measured the absorption spectra of chosen species in dichloromethane (Figure S1). Those chosen products **4** exhibited strong fluorescence emission at 480−515 nm, which suggests that this class of ionic compounds may have potential application in photoelectric materials.

Scheme 5. H/D Exchange Experiments



Scheme 6. Proposed Mechanistic Pathway of the Annulation Reaction



In conclusion, we have successfully developed a simple method for the efficient synthesis of highly substituted pyrido[1,2-*a*]quinolinium- and quinolizino[3,4,5,6-*ija*]-quinolinium-based polyheteroaromatic compounds via rhodium(III)-catalyzed multiple C−H activation annulation reactions in a one-pot process. Further mechanistic investigations and applications of the catalytic reactions are currently under investigation in our laboratory.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01055.

Full experimental procedures, optimization of reaction conditions, characterization data, and ^{1}H, ^{13}C, and ^{19}F NMR spectra of products (PDF)
Crystallographic data for **4aa** (CIF)

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Notes

The authors declare no competing financial interest.

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