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N-Doped Cationic PAHs by Rh(III)-Catalyzed Double C−H Activation and Annulation of 2-Arylbenzimidazoles with Alkynes

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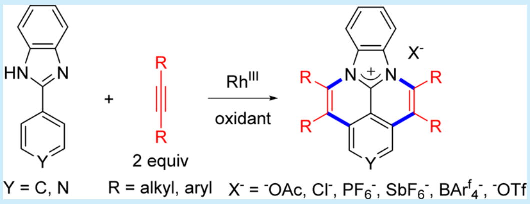
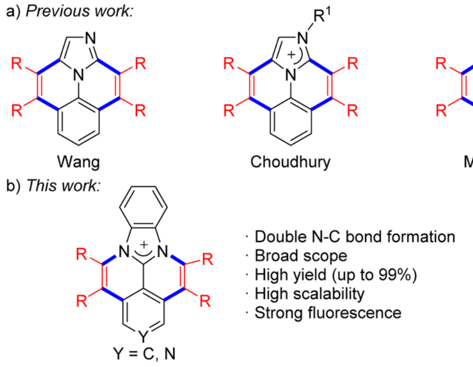
S *Supporting Information*

ABSTRACT: A novel class of N-doped cationic PAHs (polycyclic aromatic hydrocarbons) bearing the benzo[*c*,*d*]fluoranthene scaffold has been synthesized by the Rh(III)-catalyzed double-oxidative annulation of 2-arylbenzimidazoles with alkynes. The overall process involves a double C−N bond formation through a double C−H/N−H functionalization.The solid-state structures and electronic properties of the new *N*-doped PAHs were analyzed. These cationic azapolycycles were readily reduced in the presence of $LiAlH_4$ or by the addition of PhLi to give interesting phenyl and diphenylmethanediamine derivatives.



Doped polycyclic aromatic hydrocarbons (doped PAHs)[1] are considered to be a very important class of molecules in materials science due to their wide-ranging applications in electronic devices, semiconductors, solar cells, and fluorescent materials, among others. The incorporation of heteroatoms such as boron,[2] nitrogen,[3] phosphorus,[4] oxygen,[5] or sulfur[5] in the aromatic framework of PAHs can modulate their physical, chemical, and supramolecular properties. Transition-metal-catalyzed aromatic C−H activation between arenes/heteroarenes and alkynes has proven to be a powerful synthetic methodology to access different polycyclic aromatic/heteroaromatic molecules (PAHs).[6−8] Undoubtedly, nitrogen-containing derivatives are among the most abundant doped PAHs. Focusing our attention in those containing the interesting cyclopenta[*c*,*d*]phenalene unit, either neutral *N*-doped[9] or cationic derivatives have been synthesized by Wang,[7m] Choudhury,[8c] and Macgregor[7l] using Rh(III)-catalyzed double C−H activation−annulation reactions with imidazole, NHC-carbenes, and pyrazole as directing groups (Scheme 1a).[10]

Scheme 1. N-Doped Cyclopenta[*c*,*d*]phenalenes via Rh(III)-Catalyzed Double C−H Activation and Oxidative Annulation



Encouraged by these results and our interest in the behavior of amidines and guanidines as directing groups in metal-catalyzed single/multiple C−H bond activation processes,[11] we report herein the synthesis of new N-doped cationic benzo[*c*,*d*]-fluoranthene (benzimidazo[*c*,*d*]phenalene) derivatives by an efficient Rh(III)-catalyzed double-oxidative annulation of 2-arylbenzimidazoles and alkynes which involves a double C−N bond formation (Scheme 1b).

We initially tested the catalytic conditions previously reported by Miura and Satoh for the single C−H activation of 2-arylbenzimidazoles to give imidazoisoquinolines,[7a] but in the presence of 2 equiv of diphenylacetylene **2a** (Table 1).[12] However, after 24 h at 80 °C only the starting materials were recovered (Table 1, entry 1). Gratifyingly, the use of polar protic solvents had a dramatic beneficial effect on the course of the reaction since heating the mixture in MeOH at 100 °C (entry 2) led to a mixture of two products, the monocyclized imidazoisoquinoline **4aa**[7a] (66%) and the novel benzo-fused azafluoranthenium salt **3aa** (21%, air stable solid), a product derived from a double C−H/N−H functionalization that was fully characterized by single-crystal X-ray diffraction, ESI-HRMS, and NMR spectroscopy.[13] The reaction conditions were optimized to increase the selectivity of the process (entries 3−5). Thus, replacement of the oxidant $Cu(OAc)_2$ by the mixture H_2O_2/NaOAc led to a slight increase in the yield of **3aa** (entry 3). To our delight, total selectivity toward **3aa** (99%) was achieved on using AgOAc as oxidant (entry 4). Furthermore, high conversions were obtained at room temperature without compromising the yield of the reaction (entry 5).[14] A comparison between different polar protic and aprotic solvents confirmed that MeOH was the best solvent for this reaction (entries 4 and 5).[15] Other alcohols such as ^{i}PrOH or chlorinated

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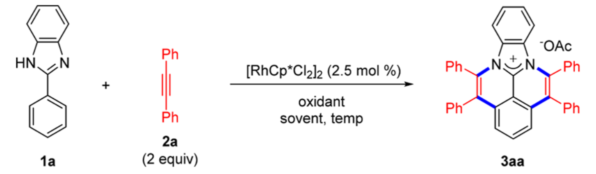
Table 1. Optimization of the Reaction Conditions[a]



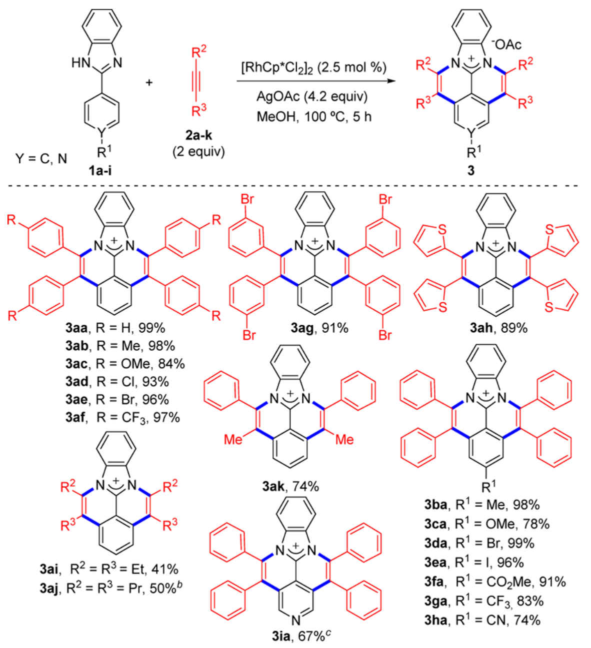
entry	oxidant	solvent	temp (°C)	time (h)	yield[b] (%)
1	$Cu(OAc)_2$	DMF	80	24	
2	$Cu(OAc)_2$	MeOH	100	24	21[c]
3	H_2O_2/NaOAc	MeOH	100	24	40[c]
4	AgOAc	MeOH	100	5	99
5	AgOAc	MeOH	25	84	87
6	AgOAc	^{i}PrOH	50	24	62
7	AgOAc	DCE	50	24	67

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (0.8 mmol), $[RhCp^*Cl_2]_2$ (2.5 mol %), oxidant (1.68 mmol), solvent (2.0 mL) in an air atmosphere unless otherwise stated. [b] Isolated yields. [c] Imidazoisoquinoline **4aa** (Scheme 3) was isolated in 66% yield (entry 2) and 55% yield (entry 3).

solvents such as 1,2-dichloroethane (DCE) gave only moderate yields (entries 6 and 7).[16] Finally, a catalyst screening showed that other metal complexes such as [Co(III)], [Ir(III)], [Pd(II)], or [Ru(II)] were totally inactive in this transformation.[15] In addition, a multigram-scale reaction was carried out with **1a** (4 mmol) to give **3aa** (2.4 g) in quantitative yield, and the catalyst loading could be reduced to 1 mol % with full conversion of the starting materials after 15 h at 100 °C.

Having identified the optimal reaction conditions, we proceeded to explore the scope of the reaction (Scheme 2). It was found that *para*-substituted aromatic alkynes were well tolerated. Both electron-donating and electron-withdrawing groups led to the corresponding *N*-doped benzo[*cd*]-fluoranthenium salts in excellent yields (**3aa**−**af**). The *meta*-substituted aromatic alkynes such as 1,2-bis(3-bromophenyl)-ethyne furnished the azafluoranthenium salt **3ag** in 91% yield.[17] Heteroaromatic alkynes such as 1,2-di(thiophene-2-yl)ethyne participate as the cycloaddition partners. One representative product, **3ah**, was formed in very good yield. Aliphatic alkynes were also successful partners under standard conditions, although moderate yields of **3ai** and **3aj**[13] were isolated since extended reaction times were required. Pleasingly, complete regioselectivity was observed with asymmetric alkynes, e.g., 1-phenyl-1-propyne, which afforded **3ak** in 74% yield.

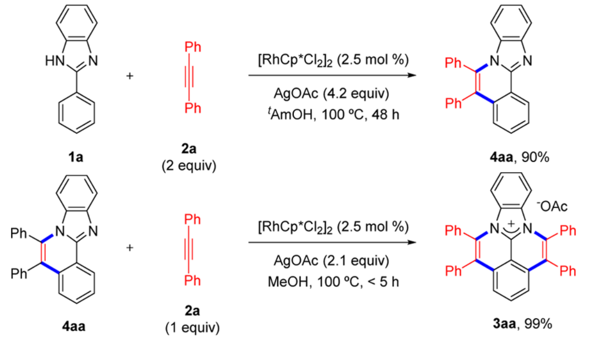
Scheme 2. Substrate Scope of the Rh^{III}-Catalyzed Double-Oxidative Annulation[a]



[a] Unless otherwise stated, all reactions were carried out using **1** (0.40 mmol), **2** (0.80 mmol), $[RhCp^*Cl_2]_2$ (2.5 mol %), AgOAc (1.68 mmol), and MeOH (2 mL) at 100 °C for 5 h. [b] 12 h. [c] 9 h.

We next analyzed the influence of substitution on the C2-phenyl ring of the benzimidazole ring. Both electron-rich and electron-poor substituents in the *para*-position allowed efficient double cycloaddition to provide the corresponding benzofused azafluoranthenium salts **3ba**−**ha** in good to excellent yields.[18] Interestingly, the reaction also tolerates halogenated substituents, i.e., Br and I, giving excellent yields of the functionalized **3da** and **3ea**, which could allow further metal-catalyzed transformations to be carried out. In addition, the reaction is also compatible with aryl groups bearing sp- and sp^2-hybridized nitrogen atoms. Thus, the nitrile derivative **3ha** could be isolated in a 74% yield, whereas the pyrido-fused azafluoranthenium salt **3ia** was obtained in 67% yield by double activation of the pyridine ring. These interesting results could allow extension of the above functionalization to other combinations of heterocycles, thus making this methodology particularly attractive for the synthesis of valuable heteroatom-doped charged PAHs.

Scheme 3. Mechanistic Studies: Double-Oxidative Annulation



As in related references,[7l,m,8c,d,10] we anticipated a similar two-step mechanism for the present catalytic reaction.[19] Thus, the reaction of **1a** with 2 equiv of **2a** in *tert*-amyl alcohol for 48 h stopped at the monocyclized imidazoisoquinoline **4aa** (Scheme 3). The yield of the dicyclized fluoranthenium salts **3** increased along the series ^{t}AmOH < ^{i}PrOH < MeOH and was zero in the first solvent and quantitative in the last solvent (see Table 1 and ref 16). This result suggests a positive solvation effect for the second C−H activation, probably due to coordination of the solvent to the Rh(III) center.[7l] On the other hand, careful monitoring of the reaction between **1a** and **2a** (2 equiv) by TLC, at short reaction times, indicated that appreciable amounts of **4aa** were not formed during the catalysis. This result is consistent with a faster reaction rate for the second C−H activation process. In an attempt to confirm the existence of **4aa** as a reaction intermediate, this compound was subjected to the optimized reaction conditions in the presence of 1 equiv of **2a**. Full conversion of **4aa** to **3aa** was observed by ^1H NMR spectroscopy in less than 5 h, and the product could be isolated in 99% yield

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(Scheme 3).[20] Finally, two different samples of either **1a** or **4aa** were charged with **2a** (2 equiv) and subjected to the optimized conditions but without the rhodium catalyst loading. After 5 h at 100 °C, only starting materials were recovered, which rules out any silver-catalyzed C−H activation process.[21]

The azafluoranthenium cations are stable with a wide variety of anions. Thus, treatment of **3·OAc** salts with saturated $NaCl_{(aq)}$ solutions and subsequent chromatography on silica gel (MeOH/CH_2Cl_2, 2%) afforded the corresponding chloride salts **3·Cl** in quantitative yield as pure microcrystalline solids. In addition, treatment of **3·Cl** with different silver salts AgX (X = PF_6, SbF_6, OTf, BAr^f_4) resulted in rapid anion exchange. Single crystals of **3aa·OAc** and **3aj·Cl** suitable for XRD analysis were obtained by slow diffusion of hexane into saturated solutions in methanol or dichloromethane/diethyl ether, respectively.

The cations present in the two salts have a pentacyclic planar structure for **3aa·OAc** and a quasiplanar structure for **3aj·Cl** (mean deviation 5.56°) (Figure 1). To the best of our knowledge, this is the first symmetrical N-doped PAH with 20π-electrons.[1c] The two C_2−N distances of 1.35 (**3aa·OAc**) and 1.36 (**3aj·Cl**) Å, which are typical in benzofused azaheterocycles, show the high symmetry of these molecules. Crystallization of the crude material after quenching the reaction between **1a** and **2a** gave a compound with a dimeric packing of two neatly stacked cations with the acetate anion, one acetic acid molecule, and a water molecule interacting within the cationic layers by hydrogen bonding. By contrast, the solid-state structure of pure **3aj·Cl** showed a dimeric packing of two cationic offset layers (interlayer space 3.33 Å)[22] with the hydrophobic propyl groups located as far as possible from one another and the chloride outside the interlayer space.

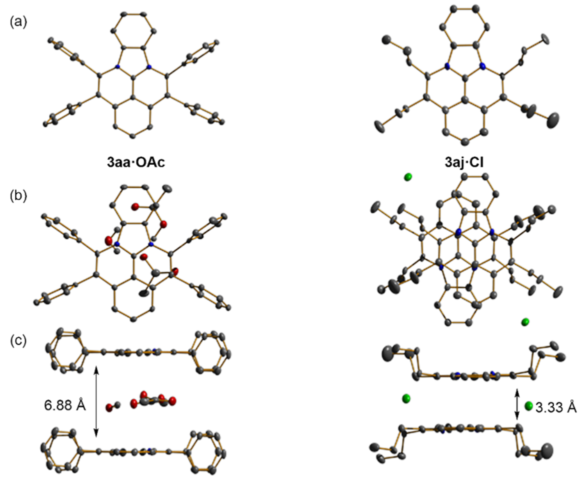


Figure 1. (a) Solid-state structures (diamond plots) of **3aa·OAc** (left) and **3aj·Cl** (right). Hydrogen atoms are omitted for clarity. Ellipsoids are drawn at the 50% probability level. 3D-dimeric packing structure viewed along the *c* axis (b) and *a* axis (c).

The UV−vis absorption and emission spectra of species **3** in CH_2Cl_2 are shown in Figure 2. The solutions were all pale yellow with strong blue-light emission under irradiation at 254 nm. In the electronic absorption spectrum, these salts showed an absolute maximum centered at around 290 nm with molar extinction coefficients that were strongly dependent on the substitution in the *para* position (Table 2). As an example, the iodo derivative **3ea·Cl** displayed a 3-fold larger ε (130000 M^{-1} cm^{-1}) than **3aa·Cl**. This parameter was also affected by the counteranion, and the maximum value was obtained for acetate.

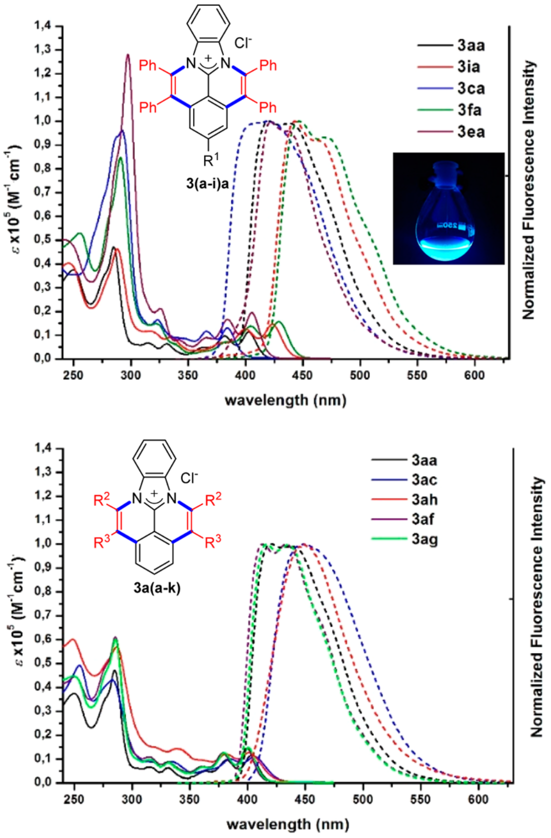


Figure 2. Electronic absorption (solid line) and electronic emission (dotted line) spectra of **3(a−i)a** (top) and **3a(a−k)** (bottom) in CH_2Cl_2.

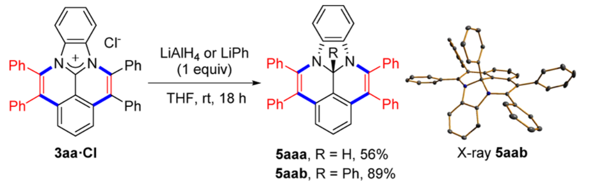
Table 2. Influence of the Anion on the Molar Extinction Coefficient

3aa·X	OAc^-	SbF_6^-	PF_6^-	$BAr^f_4{}^-$	OTf^-	Cl^-
ε(285)	77000	56800	59200	54060	53800	47100

A gradual red shift in the emission peak was observed from 415 to 470 nm as the electron-withdrawing strength of the functional group increased from **3ca·Cl** to **3fa·Cl** (Figure 2, top). The opposite effect was observed with the substitution in the *para*-position of the aromatic ring of the alkyne. Thus, a red shift from 410 to 448 nm was observed on increasing the electron-donating strength from **3af·Cl** to **3ac·Cl** (Figure 2, bottom).[15]

Interestingly, the azafluoranthenium salt **3aa·Cl** could be reduced in the presence of $LiAlH_4$ or PhLi to give phenyl- and diphenylmethanediamine derivatives **5aaa** and **5aab**[13] (Scheme 4). The former compound was extremely unstable during manipulation and gave rise to an unidentified species. In contrast, suitable crystals of **5aab**, which was stable, could be grown and

Scheme 4. Reduction of Azafluoranthenium Salt 3aa·Cl



characterized by X-ray crystallography. Formation of a tetrahedral carbon atom was accompanied by a significant modification of the electronic spectrum of **3aa·Cl**.

In summary, we have successfully developed an efficient rhodium(III)-catalyzed double-oxidative annulation between arylbenzimidazoles and alkynes to form novel N-doped benzo[*cd*]fluoranthenium salts via double C−H activation and double C−N bod formation. The new skeleton exhibits intense fluorescence, which is indicative that these compounds could have promising applications in optoelectronic materials. Further electronic studies and applications of these interesting materials 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.7b00478.

Experimental procedures and spectral data (PDF)
NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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(12) Reaction carried out in the absence of $C_5H_2Ph_4$.

(13) CCDC 1523743 (**3aa·OAc**), 1523744 (**3aj·Cl**), and 1523745 (**5aab**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre. For ORTEP diagrams of complexes **3aa·OAc**, **3aj·Cl**, and **5aab**, see the Supporting Information.

(14) Similar yields were found between reactions carried out under argon or air atmosphere.

(15) See the Supporting Information for more details.

(16) No reaction was observed in ^{t}AmOH (100 °C, 48 h) or AcOH (100 °C, 5 h).

(17) As expected, no reaction was observed with *ortho*-substituted 1,2-bis(2-bromophenyl)ethyne.

(18) The double C−H activation process was very sensitive to the steric hindrance since substrates bearing a reacting aryl ring substituted on *meta*-position give only monocyclized imidazoisoquinolines **4**. See the Supporting Information for more details.

(19) For isotopic labeling, NMR monitoring, and detailed catalytic cycle, see the Supporting Information.

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(22) Interlayer space in graphite 3.35 Å.