Organic LETTERS

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Pd-Catalyzed Intramolecular Heck Reaction, C(sp^2)−H Activation, 1,4-Pd Migration, and Aminopalladation: Chemoselective Synthesis of Dihydroindeno[1,2,3-*kl*]acridines and 3-Arylindoles

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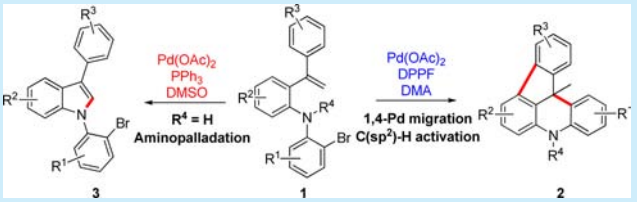
Supporting Information

ABSTRACT: Palladium-catalyzed intramolecular Heck reaction and aminopalladation of *N*-(2-(1-phenylvinyl)phenyl)-aniline for the efficient synthesis of dihydroindeno[1,2,3-*kl*]acridines and 3-arylindoles via tuning of the phosphine ligands and solvents under two optimized conditions are reported. The reaction follows a 1,4-Pd migration, aminopalladation, C(sp^2)−H activation, as well as five- and six-membered-ring fusion to form different products. The dihydroindeno[1,2,3-*kl*]acridine derivatives showed higher triplet energy (E_T) levels than common blue phosphorescent dopant and may serve as good host candidates for blue triplet emitters.



Transition-metal catalyzed direct C−H activation demonstrates a highly straightforward, efficient, and powerful method for the construction of heterocyclic compounds in organic synthesis.[1] Because of their efficient catalytic performance, palladium catalysts have been widely used in various coupling reactions to build new C−C or C−N bonds for rapid access to useful molecules and complexes.[2] Recently, palladium-catalyzed tandem intramolecular Heck reaction, 1,4-Pd migration, and C−H bond functionalization reactions have been successfully applied to construct [3,4]-fused oxindoles and 2-azabicyclo[3.3.0]octadiene derivative.[3] Therefore, it is desirable to expand this efficient strategy and design new substrates to synthesize such complex polycyclic heterocycles.

9,10-Dihydroacridine and fluorene moieties are widely present in host materials of organic light-emitting diodes (OLEDs). For example, 9,10-dihydroacridine/diphenylsulfone derivative has been successfully used as a hole transport material of excellent phosphorescent OLEDs.[4] Liao and co-workers have developed a series of host materials by incorporating 10-phenyl-9,10-dihydroacridine and fluorene moieties in a spiro linkage to fabricate blue phosphorescent OLEDs with good performance (Figure 1).[5] The Liu group has developed a series of fluorene-based oligomers with novel spiro-annulated triarylamine structures, which simultaneously solve the spectral stability problems and transport and hole-injection issues for fluorene-based blue-light-emitting materials.[6] Therefore, it is desirable to develop a new synthetic strategy to synthesize heterocycles bearing 9,10-dihydroacridine and fluorene moieties as new host materials of OLEDs.

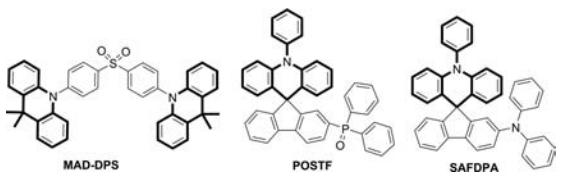
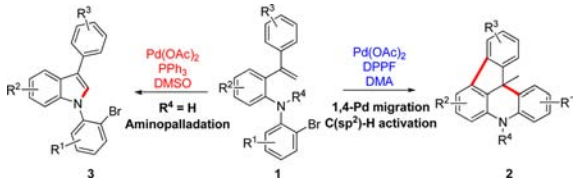


Figure 1. Host materials for organic light-emitting diodes.

Indoles are important heterocycles that exist in numerous natural products, agrochemicals, and pharmaceuticals,[7] which could be synthesized by a plethora of well-developed strategies.[8] Among them, 3-substituted indoles could be formed via direct intramolecualr amination.[9] However, it is still a challenge to construct 3-arylindoles via direct intramolecualr aminopalladation.

Herein, we describe a palladium-catalyzed intramolecular Heck reaction and aminopalladation of easily prepared *N*-(2-(1-arylvinyl)phenyl)aniline for the efficient synthesis of dihydroindeno[1,2,3-*kl*]acridines and 3-arylindoles (Scheme 1). This is achieved by tuning the phosphine ligands and solvents under two optimized conditions. The reaction underwent 1,4-Pd

Scheme 1. Palladium-Catalyzed Intramolecular Heck Reaction and Aminopalladation of *N*-(2-(1-Arylvinyl)phenyl)aniline



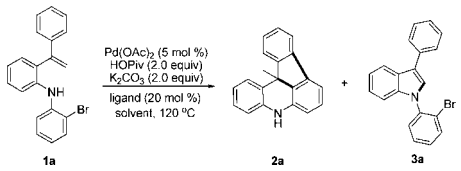
Received: March 23, 2016
Published: May 3, 2016

DOI: 10.1021/acs.orglett.6b00843
Org. Lett. 2016, 18, 2379−2382

migration, C(sp2)−H activation, and finally, five- and six-membered-ring fusion to form the products.

Initially, we attempted the reaction of 2-bromo-*N*-(2-(1-phenylvinyl)phenyl)aniline (**1a**) in *N*,*N*-dimethylacetamide (DMA) at 120 °C for 12 h, catalyzed by 5 mol % of $Pd(OAc)_2$ in the presence of 20 mol % of PPh_3, 2 equiv of K_2CO_3, and HOPiv. Surprisingly, the 1,4-migration product 12b-methyl-5,12b-dihydroindeno[1,2,3-*kl*]acridine (**2a**) and the N−H-activated product 1-(2-bromophenyl)-3-phenyl-1*H*-indole (**3a**) were obtained in 40% and 24% LC yield, respectively (Table 1, entry 1).

Table 1. Screening of Two Reaction Conditions[a]



1a 2a 3a

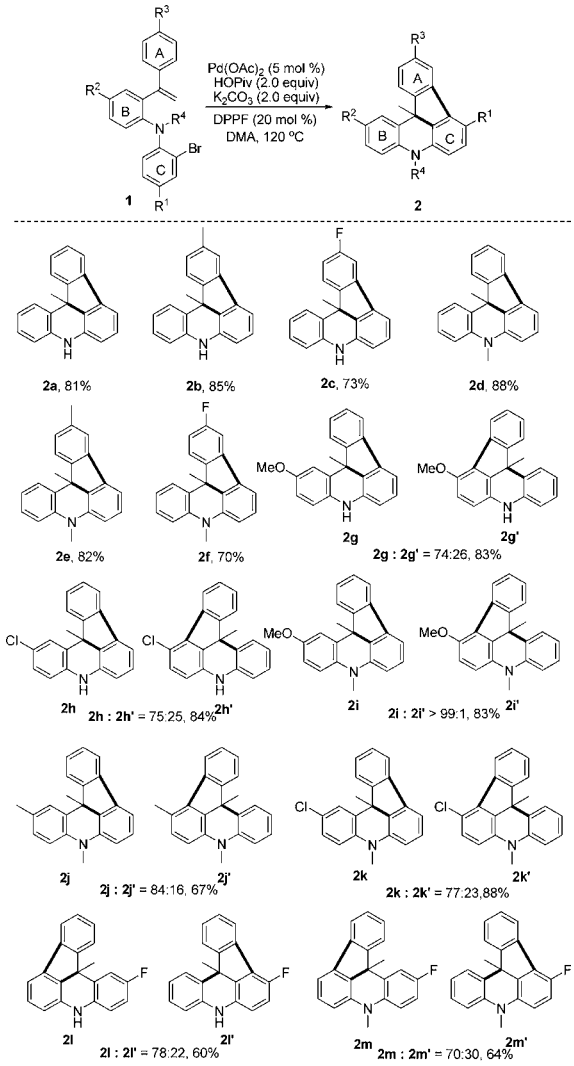
entry	cat. (5 mol %)	ligand	solvent	**2a**[b] (%)	**3a**[b] (%)
1	$Pd(OAc)_2$	PPh_3	DMA	40	24
2	$Pd(OAc)_2$	PPh_3	1,4-dioxane	39	7
3	$Pd(OAc)_2$	PPh_3	DCE	trace	trace
4	$Pd(OAc)_2$	PPh_3	toluene	32	7
5	$Pd(OAc)_2$	PPh_3	THF	6	19
6	$Pd(OAc)_2$	PPh_3	CH_3CN	14	6
7	**$Pd(OAc)_2$**	**PPh_3**	**DMSO**	**trace**	**94(88)**[c]
8	$Pd(OAc)_2$	PPh_3	DME	18	6
9	**$Pd(OAc)_2$**	**DPPF**	**DMA**	**89(81)**[c]	**trace**
10	$Pd(OAc)_2$	X-Phos	DMA	7	88
11	$Pd(OAc)_2$	$^tBu_3PhBF_4$	DMA	17	83
12	$Pd(OAc)_2$	$BuAd_2Phos$[d]	DMA	23	55
13	$Pd(OAc)_2$	Tri-O-Tphos[e]	DMA	15	74

[a]Reaction conditions: **1a** (0.5 mmol), $Pd(OAc)_2$ (5 mol %), K_2CO_3 (2.0 equiv), HOPiv (2.0 equiv), ligand (20 mol %), solvent (3 mL) at 120 °C, 12 h under air atmosphere. [b]The yields were determined by LC analysis using acetophenone as the internal standard. [c]Isolated yield. [d]$BuAd_2Phos$ = butyldi-1-adamantylphosphine. [e]Tri-O-Tphos = tris(2-methylphenyl)phosphine.

With these encouraging results, further optimization for the reaction was then carried out by employing 2-bromo-*N*-(2-(1-phenylvinyl)phenyl)aniline (**1a**) as a substrate, and the results are shown in Table 1. Screening of different solvents such as 1,4-dioxene, DCE, toluene, THF, CH_3CN, and DME indicated that these solvents did not increase the yield of the two desired products (Table 1, entries 1−6 and 8). To our delight, DMSO showed better chemoselectivity for this reaction, and **3a** was obtained in 94% yield (isolated yield 88%), together with a trace amount of **2a** (Table 1, entry 7). Next, we sought suitable reaction conditions to increase the yield of product **2a**. When different phosphine ligands were tested, most of them favored the production of **3a**, except the DPPF (1,1′-ferrocenebis(diphenylphosphine)) ligand, which led to the desired product **2a** in 89% LC yield (isolated yield 81%) and without the formation of **3a** (Table 1, entries 9−13). From the above results, we summarized two reaction conditions to afford product **2a** and **3a**, respectively. Conditions 1 for **2a**: $Pd(OAc)_2$ (5 mol %), K_2CO_3 (2.0 equiv), HOPiv (2.0 equiv), DPPF (20 mol %), DMA (3 mL) at 120 °C under air atmosphere for 12 h. Conditions 2 for **3a**: $Pd(OAc)_2$ (5 mol %), K_2CO_3 (2.0 equiv), HOPiv (2.0 equiv), PPh_3 (20 mol %), DMSO (3 mL) at 120 °C under air atmosphere for 12 h.

With the two optimal reaction conditions in hand, we investigated the reaction of a variety of *N*-(2-(1-arylvinyl)-phenyl)anilines (**1**) under conditions 1, and the results are summarized in Scheme 2. The structural variants on ring A

Scheme 2. Synthesis of Dihydroindeno[1,2,3-*kl*]acridine Derivatives[a,b]



[a]Reaction conditions: **1** (0.5 mmol), $Pd(OAc)_2$ (5 mol %), K_2CO_3 (2.0 equiv), HOPiv (2.0 equiv), DPPF (20 mol %), DMA (3 mL) at 120 °C, 12 h under air atmosphere. [b]Isolated yield; the ratio was determined by ^1H NMR analysis of the crude reaction mixture.

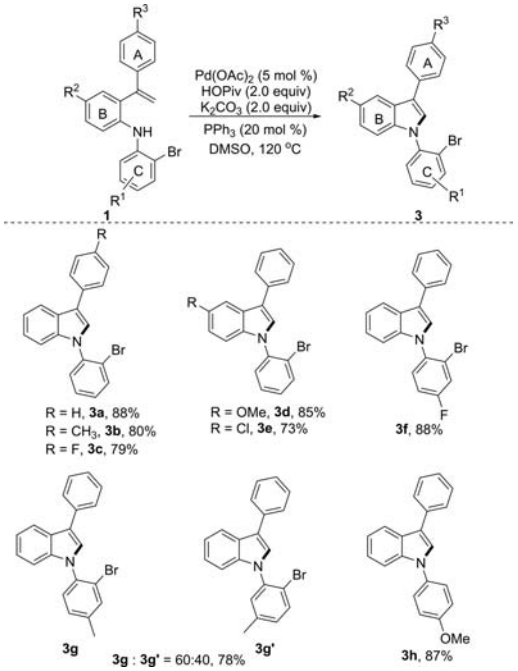
were examined first. The reaction of phenyl-substituted *N*-(2-(1-phenylvinyl)phenyl)aniline with a methyl group could afford the desired products **2b** in good yield (85%). When fluorine-benzyl-substituted aniline was subjected to the reaction conditions, the desired compound **2c** was obtained in 73% yield. The structure of **2c** was further confirmed by NMR, IR, HRMS, and X-ray analysis (see the Supporting Information).[10] Subsequently, some *N*-methyl-protected substrates such as 2-bromo-*N*-methyl-*N*-(2-(1-phenylvinyl)phenyl)aniline (**1d**), 2-bromo-*N*-methyl-*N*-(2-(1-*p*-tolylvinyl)phenyl)aniline (**1e**), and 2-bromo-*N*-methyl-*N*-(2-(1-(4-fluorophenyl)vinyl)phenyl)-aniline (**1f**) were screened, and the desired products (**2d**, **2e**,

DOI: 10.1021/acs.orglett.6b00843
Org. Lett. 2016, 18, 2379−2382

and **2f**) were all isolated in favorable yield. Next, the influence of the substitution on rings B and C was investigated. Mechanistically, the palladium complexes, generated by intramolecular Heck reaction and 1,4-palladium migration, could activate the C−H bond either on ring B or C, thus leading to the formation of two regioisomers. The cyclization then occurred preferentially at the less hindered position. For example, when ring B was substituted with a methoxy group, the reaction tended to afford **2g** as a major product (**2g**/**2g′** = 74:26). We found that when a chlorine substituent was used instead, the reaction afforded the desired product in excellent yield and regioselectivity (**2h**/**2h′** = 75:25). The *N*-methyl-protected substrates were also tested to generate the desired products **2i**−**k** in moderate yields (67−88%). The structure of **2i** was further confirmed by NMR, IR, HRMS, and X-ray analysis. Similarly, the reactions of 2-bromo-4-fluoro-*N*-(2-(1-phenylvinyl)phenyl)aniline (**1l**) and 2-bromo-4-fluoro-*N*-methyl-*N*-(2-(1-phenylvinyl)phenyl)aniline (**1m**), which have fluorine substituted on ring C, were further explored, and the desired compounds **2l** and **2m** were observed in 60% and 64% yield, respectively.

Next, we investigated the reaction scopes under the other optimized conditions to construct indoles, and the results are listed in Scheme 3. The *N*-(2-(1-phenylvinyl)phenyl)aniline

Scheme 3. Synthesis of 3-Phenylindole Derivatives[a,b]

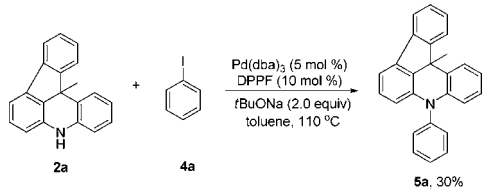


[a]Reaction conditions: **1** (0.5 mmol), $Pd(OAc)_2$ (5 mol %), K_2CO_3 (2.0 equiv), HOPiv (2.0 equiv), PPh_3 (20 mol %), DMSO (3 mL) at 120 °C, 12 h under air atmosphere. [b]Isolated yield; the ratio was determined by ^1H NMR analysis of the crude reaction mixture.

with methyl substituted on ring A could afford the desired products **3b** in 80% yield. When the fluorine-benzyl-substituted aniline was subjected to the reaction, the desired compound **3c** was obtained in 79% yield. Electron-donating (OMe) and electron-withdrawing (Cl) substituents on ring B were tested and resulted in the desired products **3d** and **3e** in 85% and 73% yield, respectively. The influence of the substitution on ring C of aniline was also examined. The fluorine substituent at the para-position improved the reaction, providing 1-(2-bromo-4-fluorophenyl)-3-phenyl-1*H*-indole (**3f**) in 88% yield. The mixture of 2-bromo-4-methyl-*N*-(2-(1-phenylvinyl)phenyl)-aniline (**1g**) and 2-bromo-5-methyl-*N*-(2-(1-phenylvinyl)-phenyl)aniline (**1g′**) (they were prepared as a mixture and **1g**/**1g′** = 62:38) also proceeded well and led to the desired products **3g** and **3g′** (60:40) in a combined 78% yield. Reaction with an electron-donating group (OMe) substituted on ring C was also carried out under the optimized conditions, and the desired product **3h** was obtained in 87% yield.

To demonstrate the utility of the current protocol, the reactions of **2a** with iodobenzene **4a** were carried out in toluene at 110 °C for 12 h, catalyzed by 5 mol % of $Pd(dba)_3$ in the presence of 10 mol % of DPPF and 2 equiv of *t*BuONa (nonoptimal conditions), and the desired product **5a** was obtained in 30% yield (Scheme 4). The two compounds

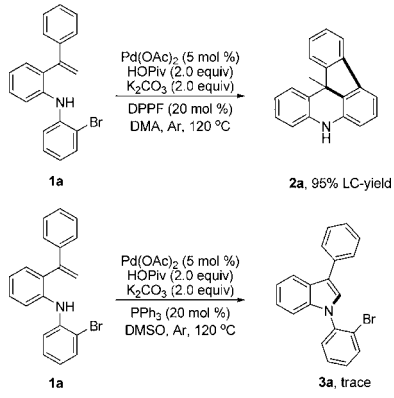
Scheme 4. Synthesis of 12*b*-Methyl-5-phenyl-5,12*b*-dihydroindeno[1,2,3-*kl*]acridine



showed higher E_T levels than common blue phosphorescent dopant, and thus, they may serve as good host candidates for blue triplet emitters (for details see Supporting Information).

To explore the plausible mechanism of the two reactions, we attempted the two experiments under Ar atmosphere (Scheme 5). For reaction 1, the product **2a** was obtained in 95% LC

Scheme 5. Control Experiment



yield, which was almost similar to the reaction performed in a closed system containing air. For reaction 2, a trace amount of product **3a** could be detected by LC−MS when the reaction was carried out under Ar atmosphere. The results showed that the former is redox-neutral (Pd(0)−Pd(II) cycle) while the latter is an oxidative transformation (Pd(II)−Pd(0) cycle requiring reoxidation of Pd(0)), and air is not necessary for the former reaction while it is essential for the latter reaction.

On the basis of the control experiments and reported literature,[11,12] a possible reaction pathway accounting for the conversion of these two reactions is depicted in Scheme 6. Oxidative addition of **1a** to Pd(0) and subsequent intramolecular Heck addition gives intermediate **A**, which is ideally

DOI: 10.1021/acs.orglett.6b00843
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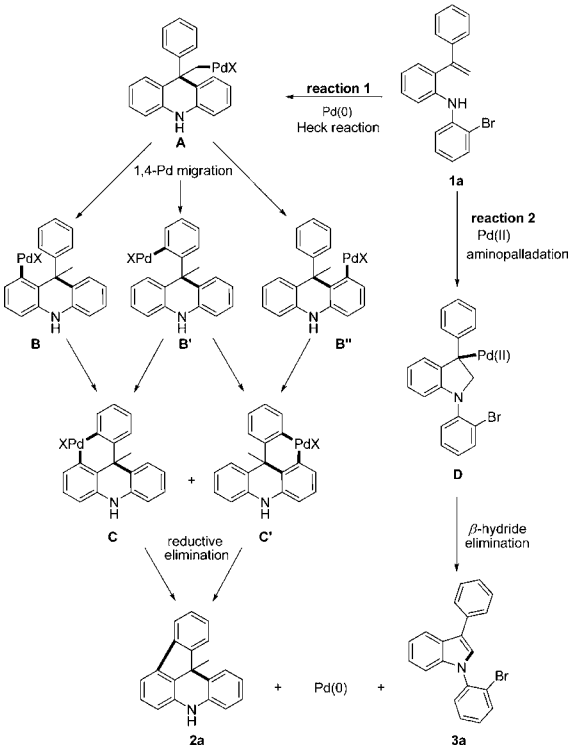
Scheme 6. Plausible Mechanism



positioned to activate the neighboring aromatic C(sp^2)−H bond. For the substrates containing three aryl groups, the 1,4-palladium migration occurs from the alkyl to the aryl position to form an arylpalladium species **B**, **B′**, or **B″**. The in situ generated Pd(II) species then activates the neighboring C4 position to afford a six-membered palladacycle **C** or **C′** (in this process, HOPiv contributes to the formation of a stable intermediate metal ring and C−H bond cleavage to the leaving proton),[11,12] which furnishes the desired product **2a** and the active Pd(0) species after reductive elimination. On the other hand, **1a** proceeds through the direct aminopalladation to generate intermediate **D**, which undergoes *β*-hydride elimination to form the desired product **3a** and the active Pd(0) species, which could be further oxidized to Pd(II) species by air.

In summary, we have developed a palladium-catalyzed intramolecular Heck reaction and aminopalladation of easily prepared *N*-(2-(1-arylvinyl)phenyl)aniline for the efficient synthesis of dihydroindeno[1,2,3-*kl*]acridines and 3-arylindoles via tuning the phosphine ligands and solvents under two optimized conditions. The reaction includes a 1,4-Pd migration, C(sp^2)−H activation, and aminopalladation, followed by the five- and six-membered-ring fusion, to afford diverse products. The dihydroindeno[1,2,3-*kl*]acridine derivatives showed higher ET levels than common blue phosphorescent dopant and might be applicable as good host candidates for blue triplet emitters.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b00843.

Detailed experimental procedures, and characterization data (PDF)

X-ray crystallographic data for **2c** (CIF)

X-ray crystallographic data for **2i** (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge the Natural Science Foundation of China (21372174, 21542015), PAPD, and Soochow University for financial support and the State and Local Joint Engineering Laboratory for Novel Functional Polymeric Materials.

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(10) CCDC 1413763 (**2c**) and 1421292 (**2i**) contain the supplementary crystallographic data for this paper. These data are available free of charge at the Cambridge Crystallographic Data Centre.

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