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A facile synthesis of indolo[3,2,1-*jk*]carbazoles via palladium-catalyzed intramolecular cyclization

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ABSTRACT

A new efficient synthesis of indolo[3,2,1-*jk*]carbazoles by the palladium-catalyzed cyclization of *N*-(2-bromoaryl)carbazoles is described. The reaction involves intramolecular C–C bond formation, coupled with the cleavage of a C–X bond and a C–H bond on carbazole ring. Substitutions on *N*-aryl core with either electron-donating or electron-withdrawing groups are introduced, and different reaction factors for cyclization are evaluated.

Organic π-conjugated oligomers and polymers with heteroatoms are useful compounds as organic functional materials which are widely applied in organic light-emitting diodes (OLEDs), organic field-effect transistors (OFETs), nonlinear optical devices (NLO), and organic solar cells. Heteroatom(s) are often contained or incorporated in these π-conjugated systems, and they generally play an important role in the properties of the materials.[1] Compounds with carbazole core such as indolo-carbazoles have been synthesized by well-defined routes. Indolo[3,2,1-*jk*]carbazoles (Scheme 1a), a special kind of indolo-carbazole positional isomers with an indolo- and a carbazole ring fused in a strained model, can be considered as aza-analogue of indeno[1,2,3-*jk*]fluorene (fluoradene, Scheme 1b). They also show quite interesting properties under electro-oxidation conditions.[2–4] Indolo[3,2,1-*jk*]carbazoles generally possess high thermostability, good fluorescence quantum yield in solution as well as strong electron donor ability, which led them promising components as charge transporting materials, conducting thin-film materials, and efficient electron donating component for fluorescent chromophores.[5]

However, there are only few reports about indolo[3,2,1-*jk*]carbazoles so far (Scheme 1). Several procedures for the construction of indolo[3,2,1-*jk*]carbazoles were reported: (1) a two-step approach by high-temperature flash vacuum pyrolysis (FVP) of 2-nitroarylcarbazoles through aryl radical pathway;[2–5] (2) a three-step route starting from the Ullmann coupling of carbazole and 1-fluoro-2-nitrobenzene, followed by the reduction and Sandmeyer process via C–H cleavage of C-1 of carbazole; (3) copper-catalyzed C–N bond formation route: heterocycles such as dibenzo[2,3:5,6]pyrrolizino[1,7-*bc*]-indolo[1,2,3-*lm*]carbazole (Scheme 1c) have been reported through C–C/C–N formation by bis-diazonium perchlorate, (4) copper-catalyzed cyclization of 5,11-bis(2-chlorophenyl)-indolo[3,2-*b*]carbazole. However, the synthesis of these compounds is hampered by the harsh reaction conditions (high temperature and high vacuum), which could cause those sensitive intermediates decomposed, or it is limited to intermediate availability. Therefore, it is worthwhile to explore novel synthetic approach to this kind of compounds due to their potentials in material chemistry.

The development of facile and efficient synthetic methodologies always plays a key role in organic synthesis. The direct arylation of arenes via C–H bond activation and halogen exchange catalyzed or mediated by transition metal catalysts has received significant attention. Palladium-catalyzed formation of carbon–carbon bonds via intramolecular C–X/C–H cross-coupling has emerged as an efficient and straightforward solution for the synthesis of a variety of heterocycles and carbocycles. Palladium-catalyzed C–H intermolecular and/or intramolecular arylation offers one of the most efficient and reliable methods for the construction of cyclic compounds.[6] Recently we have reported the synthesis of indeno[1,2,3-*jk*]fluorenes, a type of strained molecules by palladium-catalyzed intramolecular arylation through C–H activation.[7] It was previously reported that the C–H at C-1 position of carbazole ring could be activated and 6-member ring could be formed through intramolecular arylation.[8]

Considering the harsh condition or low efficiency of previous methods mentioned above, we undertook a target to establish a

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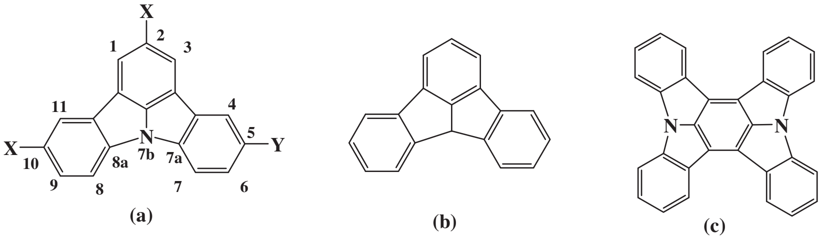
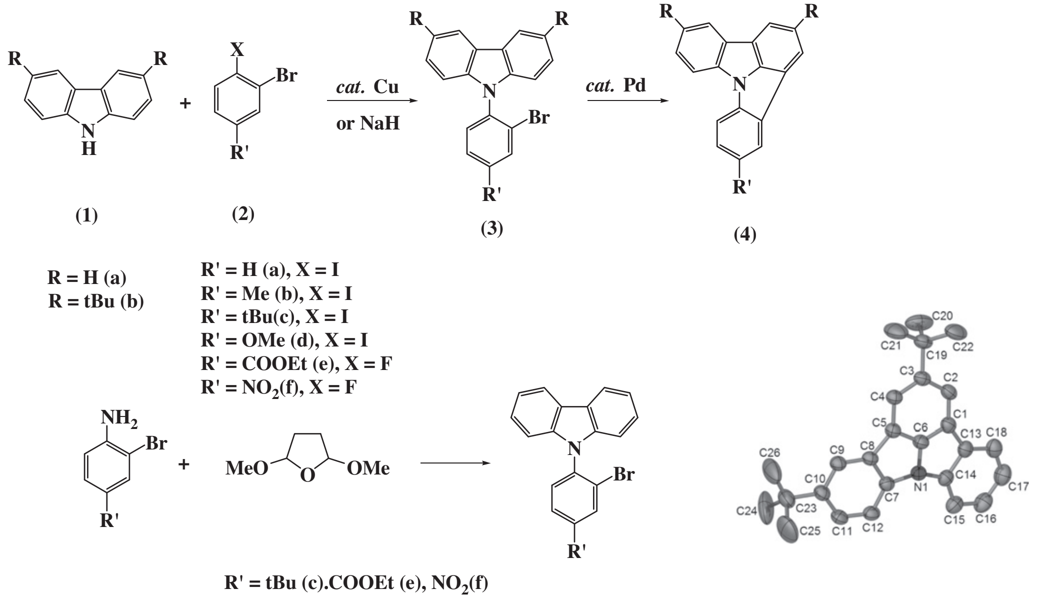
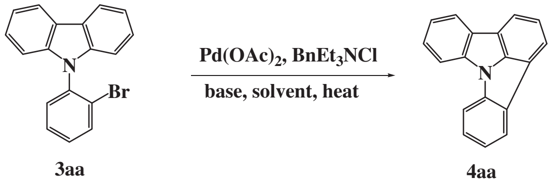


Scheme 1.



Scheme 2. Synthetic route for indolo[3,2,1-*jk*]carbazoles.



Scheme 3. Optimization of ring-closure reaction from **3aa** to **4aa**.

concise and efficient synthetic route for indolo[3,2,1-*jk*] carbazoles, which can be considered as aza-analogue of fluoradene. Based on experiences on palladium-catalyzed intramolecular arylation through C–H activation and aryl *ortho*-bromide elimination described above, we designed an alternative route for the synthesis of these strained molecules (Scheme 2). For this purpose, suitable carbazole precursors such as carbazole (**1a**) and 3,6-di-tert-butylcarbazole (**1b**) were chosen, compound **1b** could be obtained by alkylation of carbazole (69%).[9] Considering the functional group compatibility, a series of 2-bromoaryl- carbazole substrates were prepared by three major approaches: (1) most of them were obtained by copper-catalyzed Ullmann coupling of **1a** or **1b** with different compounds **2**; (2) **3ac**, **3ae**, and **3af** were obtained more efficiently by the reaction of 2-bromo-4-substituted-aniline with 2,5-dimethoxytetrafuran in refluxing glacial acetic acid; (3) **3bf** was obtained only by the reaction of **2bf** and **1b** with NaH as the base (Scheme 2).[10]

Table 1

Optimization of palladium-catalyzed cyclization of **4aa** from **3aa**

Entry[a]	Catalyst	Base	Solvent	Time[b] (h)	Yield[c] (%)
1	Pd(OAc)$_2$	Na$_2$CO$_3$	DMF	6	67
2	Pd(OAc)$_2$	Na$_2$CO$_3$	DME	14	32
3	Pd(OAc)$_2$	Na$_2$CO$_3$	1,4-Dioxane	14	17
4	Pd(OAc)$_2$	Na$_2$CO$_3$	NMP	6	60
5	Pd(OAc)$_2$	Na$_2$CO$_3$	PhMe	13	19
6	Pd(OAc)$_2$	Na$_2$CO$_3$	*p*-Xylene	13	30
7	Pd(OAc)$_2$	K$_2$CO$_3$	DMF	6	69
8	Pd(OAc)$_2$	NaHCO$_3$	DMF	6	42
9	Pd(OAc)$_2$	KHCO$_3$	DMF	6	44
10	Pd(OAc)$_2$	NEt$_3$	DMF	6	52
11	Pd(OAc)$_2$	Na$_2$CO$_3$	DMA	4	80
12	**Pd(OAc)$_2$**	**K$_2$CO$_3$**	**DMA**	**4**	**83**
13	Pd(OAc)$_2$	NaHCO$_3$	DMA	6	47
14	Pd(OAc)$_2$	KHCO$_3$	DMA	6	49
15	Pd(OAc)$_2$	NEt$_3$	DMA	6	53
16	Pd(OAc)$_2$[d]	K$_2$CO$_3$	DMA	6	66
17	Pd(OAc)$_2$[e]	K$_2$CO$_3$	DMA	6	Trace

[a] All reactions were carried out at refluxing, Pd(OAc)$_2$ (15 mol %), **3aa** (0.62 mmol), base (5 equiv), BnEt$_3$NCl (100 mol %), PPh$_3$ (35 mol %), and solvent (50 mL).

[b] Reaction time for consumption of **3aa** by thin layer chromatography (TLC).

[c] Isolated yield.

[d] Pd(OAc)$_2$ (10 mol %).

[e] Pd(OAc)$_2$ (5 mol %).

The intramolecular arylation coupling reaction was initially screened with substrate **3aa** by using a protocol by us[7] and others[8]

Table 2
Indolo[3,2,1-*jk*]carbazoles

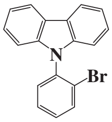
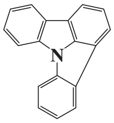
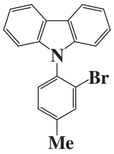
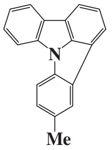
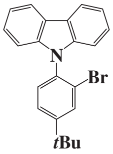
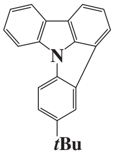
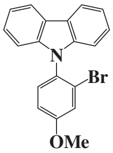
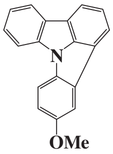
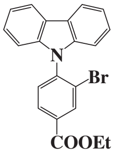
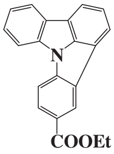
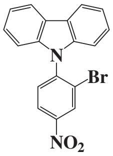
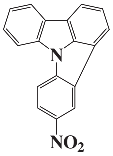
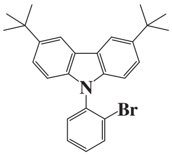
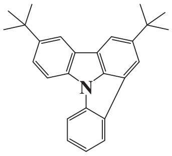
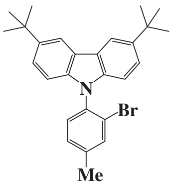
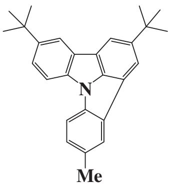
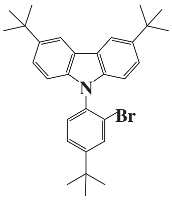
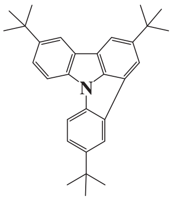
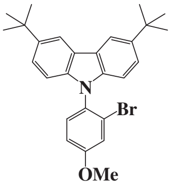
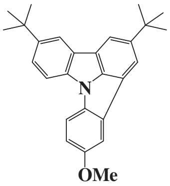
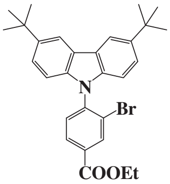
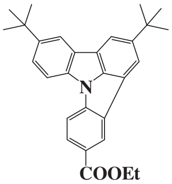
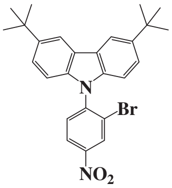
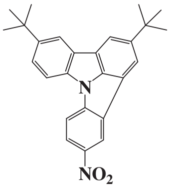
Entry	Precursor	Indolo[3,2,1-*jk*]carbazole	Time (h)	Yield[a] (%)
1	 **3aa**	 **4aa**	6	83
2	 **3ab**	 **4ab**	6	80
3	 **3ac**	 **4ac**	6	70
4	 **3ad**	 **4ad**	6	66
5	 **3ae**	 **4ae**	12	43
6	 **3af**	 **4af**	12	29
7	 **3ba**	 **4ba**	6	83
8	 **3bb**	 **4bb**	6	80
9	 **3bc**	 **4bc**	6	71

Table 2 (*continued*)

Entry	Precursor	Indolo[3,2,1-*jk*]carbazole	Time (h)	Yield[a] (%)
10	 **3bd**	 **4bd**	6	–[b]
11	 **3be**	 **4be**	12	43
12	 **3bf**	 **4bf**	12	28

[a] Isolated yield.

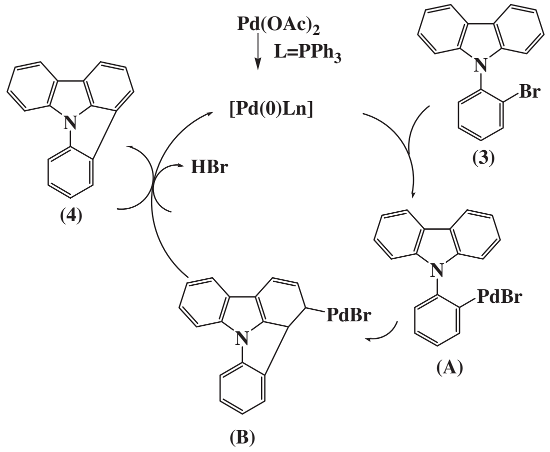
[b] Dehalogenated by–products formed. See Supplementary data for detail.

in the presence of $Pd(OAc)_2$ as catalyst, Na_2CO_3 as base, and $BnEt_3NCl$ as additive in refluxed *N,N*-dimethylformamide (DMF) under nitrogen atmosphere, the reaction proceeded smoothly, the starting materials were totally converted within 6 h, and the target compound **4aa** was obtained with an isolated yield of 67% (Scheme 3, Table 1, entry 1).

Therefore, we performed a list of experiments with focus on precursor **3aa** where sequential changes were made to solvents, base, and catalyst loadings for the optimization of the reaction conditions. We examined several solvents such as DMF, *N,N*-dimethylacetamide (DMA), dimethoxyethane (DME), 1,4-dioxane, *N*-methylpyrrolidene (NMP), toluene, and *p*-xylene and found the cyclization could be proceeded both in polar and non-polar solvents, among the solvents considered, DMA afforded the best results (83%, Table 1, entry 12).

The effect of base was also studied both in DMF and DMA, K_2CO_3 was found to be superior to other four bases (Na_2CO_3, $NaHCO_3$, $KHCO_3$, Et_3N) examined both in DMF and DMA (Table 1, entries 7 and 11). Then we secured the solvent and base for further evaluation. As for catalyst loading, we found that the isolated yields of **4aa** are almost the same when $Pd(OAc)_2$ was taken 15–30 mol %. However, when the catalyst loading was decreased to 5 mol % there is only trace of the desired product (as shown by TLC, Table 1, entry 17), which could not be isolated. While the catalyst loading was changed to 10 mol %, the yield was increased to 66% (Table 1, entry 16). Therefore conditions involving 15 mol % of $Pd(OAc)_{2,}$ 35 mol % of PPh_3, 1 equiv of $BnEt_3NCl$, 5 equiv of K_2CO_3 in refluxing DMA were selected to the generality of this method for further synthesis of other indolo[3,2,1-*jk*]carbazoles.

With optimized conditions in hand, we set out to examine the general scope of the reaction (Table 2). The 12 substrates **3aa–3bf** with different substituents were examined, we found the cyclization could be proceeded within 6 h for most of them, the target molecules could be isolated in fair to good yields when the substituents are H, Me, *t*Bu, and OMe, while those substrates with electron withdrawing groups at *para*-position of phenyl ring could also be finished in longer time (*ca.* 12 h) with dropped isolated yields (28–43%, Table 2 entries 5–6, 11–12).



Scheme 4. Plausible mechanism for Palladium-catalyzed cyclization.

The proposed mechanism for palladium-catalyzed cyclization toward indolo[3,2,1-*jk*]-carbazoles is shown in Scheme 4 (with the formation of 4aa as e.g.). Presumably, initially oxidative addition of **3** with palladium might form aryl-palladium intermediate (**A**), followed by addition to the double bond of carbazole ring to give intermediate (**B**), the β-hydrogen elimination is triggered by attack of bases to aromatic protons to form compound **4**.[6–8]

In summary, we have described a novel approach to indolo[3,2,1-*jk*]carbazoles with various functional groups by palladium-catalyzed transformation, where N-(2-bromoaryl)carbazoles are cyclized to give the target molecules via C–X/C–H cross-coupling. Palladium facilitates the formation of *an aromatic palladium bromide* by oxidation addition, while the base provides the driving force for carbon–carbon bond formation of the expected indolo[3,2,1-*jk*]carbazoles in either polar or non-polar solvents. The application of these compounds as electron-donating components in material chemistry is now undergoing.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.07.093.

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10. See Supplementary data for details.