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A base-free, one-pot diazotization/cross-coupling of anilines with arylboronic acids

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ABSTRACT

Pd-catalyzed one-pot diazotization/cross-coupling is realized for the synthesis of biaryls directly from anilines and arylboronic acids.

Suzuki–Miyaura cross-coupling is a powerful tool for the construction of C–C bonds.[1] In general, aryl halides or triflates are used as coupling partners. The search for alternative electrophilic coupling partner continues to attract interests among the synthetic organic community.[2] Arenediazonium salts represent an attractive alternative due to their high reactivity and easy availability from aniline derivatives.[3–7] The first utilization of the aryldiazonium salts as electrophiles in palladium-catalyzed Suzuki–Miyaura cross-couplings was achieved independently by Genet[4] and Sengupta.[5] These investigations allow biaryls synthesis with moderate to good yields by coupling of aryldiazonium tetrafluoroborates and arylboronic acids in the presence of catalytic amounts of $Pd(OAc)_2$ and without adding base and ligands. In 2001, Andrus and Song reported a palladium-imidazolium carbene catalyst system for the cross-coupling of arylboronic acid with aryldiazonium tetrafluoroborates. The reaction could be carried out at low temperature (0 °C or room temperature) and afforded the coupling products with high yields.[6]

Although aryldiazonium tetrafluoroborates have been well established as coupling partners in Pd-catalyzed reactions, there are some drawbacks. First, aryldiazonium tetrafluoroborates are generally unstable and only few of them are commercially available. Therefore, they should be newly prepared before use. However, the procedure for the preparation of aryldiazonium tetrafluoroborates is hazardous and tedious due to the use of fluoroboric acid and recrystallization in separation process.[8] As a result, the reaction usually gives low yield especially when carried out in a small scale. Consequently, the advantage of easy availability of aniline starting materials may be counteracted by the lack of efficiency and flexibility in the preparation of aryldiazonium tetrafluoroborates.

We conceived that a one-pot diazotization/cross-coupling would circumvent these setbacks. Such an approach has been pursued first by Fujiwara and coworkers in 1980,[9] although in their seminal work stoichiometric amount of $Pd(OAc)_2$ was required in order to obtain good yields. Almost at the same time, Matsuda and coworkers described the same coupling reaction but using alkyl nitrite as diazotizing agent and catalytic amounts of $Pd_2(dba)_3$.[10] Andrus and Song have also demonstrated the one-pot diazotization/cross-coupling in their catalytic system with palladium-imidazolium carbene as catalyst.[6] Encouraged by these developments, we wish to report in this Letter an efficient Pd-catalyzed base-free cross-coupling of arylamines and arylboronic acids with *tert*-butyl nitrite as diazotizing agent.[11] The reaction does not need to use $BF_3{\cdot}OEt_2$ as in the case of Andrus's system.

Initial screening of the reaction conditions with aniline **1a**, *p*-tolylboronic acid **2a**, and *tert*-butyl nitrite revealed that the usual Suzuki–Miyaura coupling protocol [DME, $Pd(PPh_3)_4$, aqueous Na_2CO_3] failed to afford any desired product. After some experimentations, it was concluded that the desired cross-coupling product **3a** could be obtained in 36% GC–MS yield under a condition with 5 mol % $Pd(PPh_3)_4$ in CH_3CN at 90 °C (Table 1, entry 1). Encouraged by this initial result, we further proceeded to optimize the reaction conditions. First, different solvents were examined and it was concluded that DMF afforded the best yield of 64%

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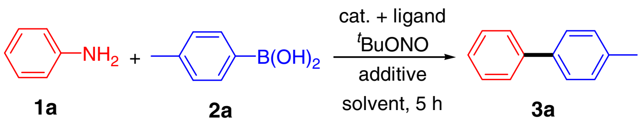
Table 1
Pd-catalyzed cross-coupling of aniline **1a** and *p*-tolylboronic acid **2a**[a]

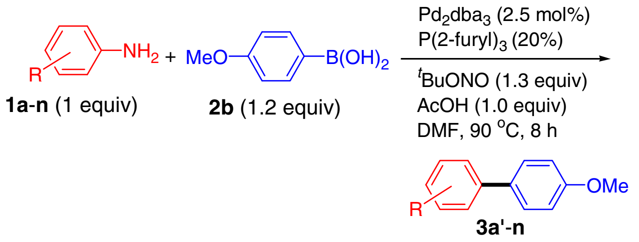


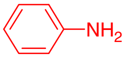
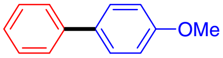
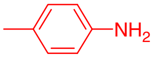
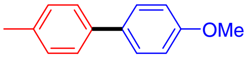
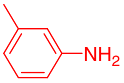
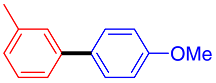
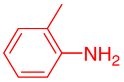
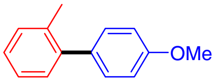
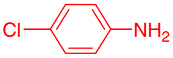
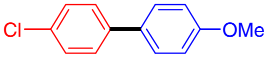
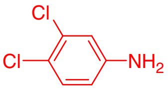
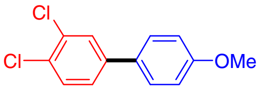
Entry	Cat. (mol %)	Solvent (mol %)	Additive	Temp (°C)	Yield[b] (**3a**, %)
1	$Pd(PPh_3)_4$(5)	MeCN	–	90	36
2	$Pd(PPh_3)_4$(5)	DCE	–	90	8
3	$Pd(PPh_3)_4$(5)	Toluene	–	90	17
4	$Pd(PPh_3)_4$(5)	DMSO	–	90	52
5	$Pd(PPh_3)_4$(5)	DMF	–	90	64
6	–	MeCN	–	90	0
7	$Pd(PPh_3)_4$(5)	DMF	K_2CO_3 (200)	90	8
8	$PdCl_2(PPh_3)_2$(5)	DMF	–	90	12
9	$Pd(P^tBu)_3$(5)	DMF	–	90	32
10	$Pd(OAc)_2$(5)	DMF	–	90	17
11	$Pd(PPh_3)_4$(5)	DMF	–	90	49
12	$Pd(PPh_3)_4$(5)	DMF	AcOH (100)	90	70
13	Pd_2dba_3(2.5)/P(2-furyl)$_3$(15)	DMF	–	90	74
14	Pd_2dba_3(2.5) P(2-furyl)$_3$(15)	DMF	AcOH (100)	90	91

[a] Reaction conditions: aniline **1a** (0.5 mmol); **1a**:**2a**:^{t}BuONO = 1:1.3:1.2; solvent 2 mL, under N_2.

[b] GC–MS yield using mesitylene as internal standard.

Tab1e 2
The scope of the one-pot diazotization-coupling reaction[a]



Entry	Arylamines **1a**–**n**	Products **3a′**–**n**	Yield[b] (%)
1	 **1a**	 **3a'**	81
2	 **1b**	 **3b**	77
3	 **1c**	 **3c**	73
4	 **1d**	 **3d**	52
5	 **1e**	 **3e**	75
6	 **1f**	 **3f**	56

(*continued on next page*)