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Palladium-catalyzed direct allylation of fluorinated benzothiadiazoles with allyl chlorides

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ABSTRACT

A palladium catalyzed cross-coupling of fluorinated benzothiadiazoles (FBTs) with allyl chlorides is reported. The significant feature of this method is synthetic simplicity, providing a straightforward access to unsymmetrical and symmetrical alkylated FBT derivatives that are of interest in organic electronic and optoelectronic materials.

1. Introduction

Organic molecules bearing donor-acceptor moieties have found wide application in organic electronic and optoelectronic materials [1]. Over the past decade, various electron deficient aromatics (acceptor) have been prepared to develop high performance advanced functional materials. Among them fluorinated benzothiadiazoles (FBTs), such as 5, 6-difluoro-benzothiadiazole (DFBT) and 5-fluoro-benzothiadiazole (MFBT), have gained extensive attention [2] due to the unique properties of fluorine atom. It has been demonstrated that the introduction of fluorine atom(s) into the acceptor not only can improve the interactions between electron rich nonfluorinated aromatics and fluorinated electron deficient aromatics, but also can lower the HOMO and LUMO levels of conjugated molecules [3]. In this regard, many organic materials containing FBT motifs have been developed [2]. Commonly, FBT derivatives are prepared from the cross-coupling of dihalogenated FBTs with (hetero)arylstannanes [4] or with (hetero)arylboron reagents [5]. However, these multi-prefunctionalization processes of both coupling partners suffer from intrinsic drawbacks in terms of atom and step economy. Furthermore, this prefunctionalization strategy for the preparation of FBT derivatives often produces symmetrical disubstituted FBTs, in which an unstable 4,7-diiodo-DFBT [6] are usually required, thus limiting their widespread synthetic applications.

To address these issues, recently, we developed a straightforward strategy for direct (hetero)arylation [7,8] and olefination [9] of FBTs by a palladium catalysis. To continue our research in this area [10], herein, we describe an efficient method for direct C–H bond allylation of FBTs catalyzed by palladium. The reaction proceeds under mild reaction conditions with high efficiency and good functional group tolerance, providing a facile route to access unsymmetrical FBT derivatives.

2. Results and discussion

We began this study by choosing 5, 6-difluoro-4-bromo benzothiadiazole **1a** [7] and cinnamyl chloride **2a** as model substrates (Table 1). The use of **1a** is because of its synthetic versatility, which can enrich the structural diversity of FBTs after the downstream transformations of its C–Br bond. Initially, no desired product **3a** was observed when **1a** was treated with **2a** in the presence of $Pd(OAc)_2$ (10 mol%), PPh_3 (20 mol%), and K_2CO_3 (1.2 equiv) in toluene at 120 °C (entry 1). After a survey of the reaction parameters, including palladium sources, ligand, base, solvent and reaction

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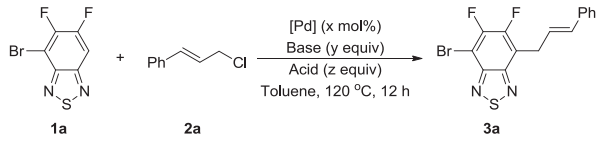
Table 1
Representative results for the optimization of palladium-catalyzed direct allylation of **1a** with **2a**.[a]



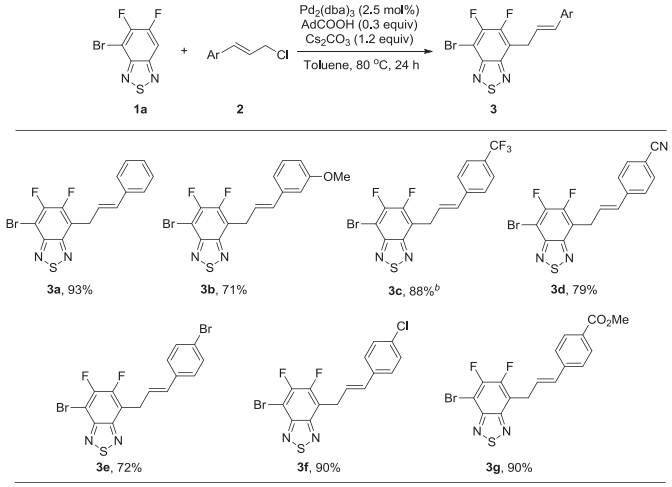
Entry	[Pd] (x)	Base (y)	Acid (z)	3a Yield[b] (%)
1[c]	$Pd(OAc)_2$, 10	K_2CO_3, 1.2	/	ND
2	$Pd(OAc)_2$, 10	K_2CO_3, 1.2	/	70
3	$[PdCl(C_3H_5)]_2$, 5	K_2CO_3, 1.2	/	60
4	$Pd(PPh_3)_4$, 10	K_2CO_3, 1.2	/	ND
5	$Pd_2(dba)_3$, 5	K_2CO_3, 1.2	/	75
6	$Pd_2(dba)_3$, 5	Na_2CO_3, 1.2	/	36
7	$Pd_2(dba)_3$, 5	*t*BuOLi, 1.2	/	ND
8	$Pd_2(dba)_3$, 5	Cs_2CO_3, 1.2	/	88
9[d]	$Pd_2(dba)_3$, 5	Cs_2CO_3, 1.2	/	89
10[d]	$Pd_2(dba)_3$, 5	Cs_2CO_3, 2.4	$PhCO_2H$, 1.2	67
11[d]	$Pd_2(dba)_3$, 5	Cs_2CO_3, 2.4	*o*-$MePhCO_2H$, 1.2	88
12[d]	$Pd_2(dba)_3$, 5	Cs_2CO_3, 2.4	*m*-$MePhCO_2H$, 1.2	60
13[d]	$Pd_2(dba)_3$, 5	Cs_2CO_3, 2.4	$AdCO_2H$, 1.2	91
14[d]	$Pd_2(dba)_3$, 5	Cs_2CO_3, 1.2	$AdCO_2H$, 0.3	92
15[d,e]	$Pd_2(dba)_3$, 2.5	Cs_2CO_3, 1.2	$AdCO_2H$, 0.3	94 (93)

[a] Reaction conditions (unless otherwise specified): **1a** (0.45 mmol), **2a** (0.3 mmol, 1.0 equiv), toluene (1 mL), 12 h.
[b] Yield determined by ^{19}F NMR using fluorobenzene as an internal standard and number in parenthesis is isolated yield, ND = yield not determined.
[c] 20 mol% PPh_3 was used.
[d] The reaction was conducted at 80 °C for 24 h.
[e] **1a** (0.9 mmol), **2a** (0.6 mmol), toluene (3.0 mL).

temperature, we found that the phosphine ligand had a negative effect on the reaction efficiency (for details, see the Supporting Information, SI). While, the absence of phosphine ligand could afford **3a** in 70% yield (entry 2). Among the tested palladium sources (entries 3–5), $Pd_2(dba)_3$ could improve the yield of **3a** to 75% (entry 5), but $Pd(PPh_3)_4$ led to no product due to the existence of phosphine ligand (entry 4). The choice of base is critical to the reaction efficiency (entries 6–8) and 88% yield of **3a** was produced with Cs_2CO_3 as a base (entry 8). The reaction is also sensitive to the nature of solvent. Polar solvents, such as DMF, NMP and DMSO, and ethereal solvents, including dioxane and DME, all failed to provide **3a** (SI). Decreasing the reaction temperature to 80 °C did not affect the reaction efficiency and a comparable yield of **3a** was still obtained. To optimize the reaction conditions further, a range of carboxylic acids, which previously were proved to have a beneficial effect on C–H bond functionalization, were examined (entries 10–13) [11]. Finally, the highest yield of **3a** (93%) was obtained by decreasing the loading amount of $Pd_2(dba)_3$ to 2.5 mol% with 1.2 equiv of Cs_2CO_3 as a base and 0.3 equiv of $AdCO_2H$ as an additive (entry 15).

With the optimal reaction conditions in hand, we then examined the substrate scope of this method with a variety of allyl chlorides (Table 2). Generally, good to high yields of **3** were obtained with high *regio*- and *E*-stereoselectivities. The *E*-configuration of **3** was assigned by the ^1H NMR, in which the proton coupling constants (*J*) of *E*-configuration HC=CH range from 15.1 to 15.9 Hz. Remarkably, many important functional groups, such as cyano, chloride, bromide and ester showed good tolerance to the reaction. Most importantly, the successful direct allylation of **1a** with intact Ar–Br bond provides good opportunities for downstream transformations of resulting allylic products, thus demonstrating the advantage of this protocol. For example, the dibrominated product

Table 2
Palladium-catalyzed direct allylation of **1a** with **2**.[a]

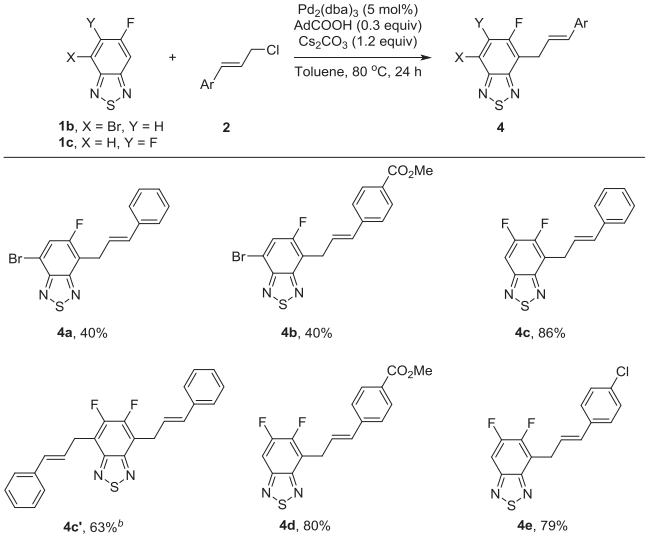


[a] Reaction conditions (unless otherwise specified): **1a** (0.9 mmol, 1.5 equiv) and **2** (0.6 mmol, 1.0 equiv) in toluene 3.0 mL, 80 °C, 24 h. Isolated yields. [b] 5 mol% $Pd_2(dba)_3$ was used.

3e may serve as a versatile building block for the preparation of new interesting advanced functional materials.

The reaction can also be extended to monofluorinated benzothiadiazole **1b** and nonbrominated difluorinated benzothiadiazole **1c** (Table 3). Synthetically useful yields were obtained when **1b** was examined (**4a** and **4b**). The relatively low reactivity of **1b** comparing to **1a** is probably because of its absence of one fluorine atom, which decreases the acidity of the C–H bond *ortho* to the fluorine atom [9a,12]. However, compound **1c** showed good reactivity. Notably, the di- and mono-allylation of **1c** can be modulated by the ratio between **1c** and allyl chlorides **2**. Increasing the ratio of **1c**/**2** to 3:1

Table 3
Palladium-catalyzed direct allylation of **1b** or **1c** with **2**.[a]



[a] **1** (1.8 mmol, 3.0 equiv), **2** (0.6 mmol, 1.0 equiv), toluene (3.0 mL), isolated yields. [b] **1c** (0.6 mmol), **2a** (1.2 mmol), toluene (3.0 mL), isolated yield.

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