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Palladium-catalyzed cross-coupling of aryldiazonium tetrafluoroborate salts with arylboronic esters

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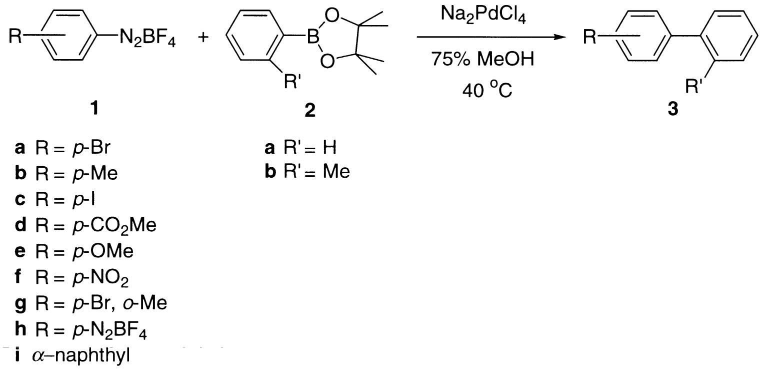
Abstract

A novel palladium-catalyzed reaction of aryldiazonium tetrafluoroborate salts with arylboronic esters furnishes cross-coupled products in moderate yields. The reaction proceeds at relatively mild temperatures and in aqueous media. © 2000 Published by Elsevier Science Ltd.

Palladium-catalyzed coupling reactions have attracted significant attention during the past two decades.[1] Of recent interest is the palladium-catalyzed cross-coupling of aryldiazonium tetrafluoroborate salts with arylboronic acids[2]. In addition, aryldiazonium tetrafluoroborate salts have also been successfully cross-coupled to organotrifluoroborates.[3] Suitable conditions for the successful direct, catalytic cross-coupling of aryldiazonium tetrafluoroborate salts to arylboronic esters, however, had not been found.[4]



Scheme 1.

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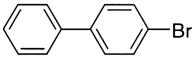
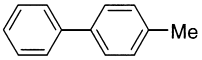
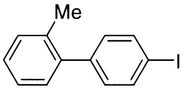
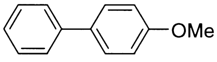
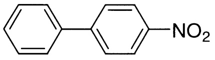
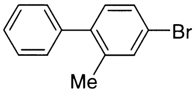
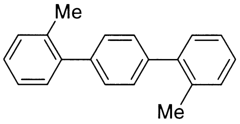
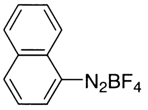
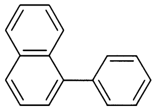
The relatively mild preparation of arylboronic esters tolerates a broad range of functional groups[5] and affords access to one-pot conversion to cross-coupled products.[6] The diazonium electrophile, which can be synthesized from inexpensive, readily available anilines, is the most powerful nucleofuge used in differential cross-couplings.[7] The cross-coupling of aryldiazoniums with arylboronates would thus be of broad synthetic utility. As part of our program towards efficient syntheses of well-defined oligoaromatic materials[8] for sensory applications,[9] we decided to explore the palladium-catalyzed cross-coupling of aryldiazonium tetrafluoroborate salts **1**[10] with arylboronic esters **2** (Scheme 1). Herein we report our preliminary findings concerning the synthesis of unsymmetric biaryls in moderate yields in aqueous MeOH, at mild temperatures.

We initially screened the reaction of **1a** (1.0 mmol) and **2a** (1.5 mmol) in a variety of solvents (2 mL) in the presence of CsF or KF (2 equiv.)[11] at room temperature for 24 h, employing $PdCl_2$ (5–10 mol%) as the catalyst. We monitored reaction progress by GC/MS. In anhydrous or 50%

Table 1
Cross-coupling of aryldiazonium tetrafluoroborate salts **1** with arylboronic esters **2**

Entry	1	2	3		% Yield[a]
1	1a	2a		3a	56
2	1b	2a		3b	62
3	1c	2b		3c	66
4	1d	2a		3d	61
5	1e	2a		3e	54
6	1f	2a		3f	64
7	1g	2a		3g	48
8	1h	2b		3h	16
9		2a		3i	64

[a] Isolated yield.

aqueous MeOH solvent, complete consumption of starting materials and the best relative conversion (54%) to cross-coupled product **3a** was observed in these initial attempts. The polar aprotic solvents DMF and MeCN led to only trace consumption of starting materials. In two anhydrous polar aprotic solvents (THF or Me_2CO), no reaction occurred; however, with 50% aqueous solutions of THF or Me_2CO we observed complete consumption of starting materials.[12] Based on these findings, we decided to study the cross coupling of several aryldiazonium tetrafluoroborate salts with arylboronates using 75% MeOH as the solvent, CsF as the base and the more aqueous soluble Na_2PdCl_4 as the catalyst (Table 1).

As shown in Table 1, the cross-coupling reactions, after 20–24 h at 40°C under inert atmosphere afforded unsymmetric biaryls **3** in moderate yields.[13] Aryldiazonium tetrafluoroborate salts **1** containing electron donating, electron withdrawing or sterically encumbered *ortho*-substituted moieties furnished cross-coupled products. The reaction of 4-iodophenyldiazonium tetrafluoroborate salt **1c** with **2b** furnished 4-iodo-2′-methylbiphenyl **3c** as the only cross-coupled product, highlighting the outstanding regioselectivity afforded by the diazonium moiety.

In conclusion, the current study demonstrates that readily available aryldiazonium tetrafluoroborate salts react with functional group tolerant arylboronic esters in aqueous solvents at mild temperatures to form isolable cross-coupled products. Ongoing optimization studies are aimed at further elucidating the mechanism, scope and limitations of the reaction.

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12. A mixture of desired product **3** and homocoupled by-products characteristically precipitates from these reactions under the described aqueous conditions.
13. General procedure for cross-coupling of aryldiazonium tetrafluoroborate salts **1** and arylboronic esters **2**. Aryldiazonium tetrafluoroborate salt (1.0 mmol), arylboronic ester (1.5 mmol), Na_2PdCl_4 (0.10 mmol) and CsF (1.5 mmol) were added to a reaction vessel purged thoroughly with N_2 in the dark. Degassed 75% MeOH/H_2O (2 mL) was added via syringe and the reaction was allowed to proceed at 40°C in a sand bath until completion. The solution was cooled to room temperature, concentrated, and the residue extracted with EtOAc (3×10 mL). The organic layer was dried with $MgSO_4$, passed through Celite and the filtrate concentrated. Silica gel chromatography (pentane or 0–10% EtOAc in hexanes) afforded the respective biaryls, **3a**–**g**, terphenyl **3h** and naphthyl derivative **3i**. Physical data for the cross-coupled products were consistent with the literature: the purity of each product was verified by GC/MS (tetradecane internal standard) and ^{1}H NMR. Alkyl- and benzyldiazonium tetrafluoroborate salts were unreactive under these conditions.