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Cross-Coupling of Arenediazonium Tetrafluoroborates with Arylboronic Acids Catalysed by Palladium

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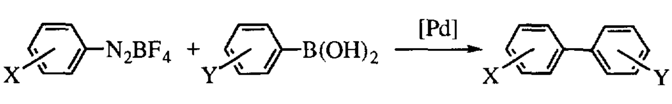
Abstract : Suzuki cross-coupling of various arenediazonium tetrafluoroborates and arylboronic acids is described for the first time in the presence of a catalytic amount of $Pd(OAc)_2$, at ambient temperature and in the absence of both base and phosphine ligand. Copyright © 1996 Elsevier Science Ltd

Cross-coupling reactions between electrophilic and nucleophilic aromatic partners catalysed by palladium have gained a great interest in the last two decades and they constitute a powerful synthetic tool[1]. Among the various methods to prepare unsymmetrical biaryls, the most widely used are the palladium-catalysed cross-coupling of arylstannanes (Stille coupling)[2] and arylboronic acids or esters (Suzuki coupling)[3] with an aryl halide or sulfonate. Because of the economic advantage of anilines over arylbromides or iodides, and in our continuing interest in palladium-catalysed reactions[4], we turned our attention to the coupling of arenediazonium salts with arylboronic acids. Recently, the palladium-catalysed coupling of arenediazonium salts has been achieved with alkenes[5], organostannanes[6], silyl, germyl and stannyl alkenes[7], as well as palladium-catalysed carboxylation[8], formylation[9] and carbonylation[10].

We wish to report herein the first cross-coupling reaction between arenediazonium tetrafluoroborates and arylboronic acids.

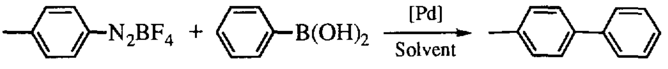


X = Me, OMe, CO_2Et, COPh, Br
Y = H, OMe, Cl, F

Initially, we examined the cross-coupling of 4-methylbenzenediazonium fluoroborate **1** with phenylboronic acid **2** in neutral medium. As shown in Table 1, the expected 4-methylbiphenyl **3** is obtained at room temperature in the presence of a catalytic amount of $Pd(OAc)_2$ and in the absence of base.

The reaction yields are greatly influenced by the solvent employed. A careful examination of various reaction conditions shows that ethereal solvents are the most suitable (entry 5-7), particularly 1,4-dioxane (entry 7). In protic solvents (entry 1 and 2) important quantities of by-products are formed, including toluene and 4,4'-dimethylbiphenyl which result respectively from the reduction and the homocoupling of the diazonium salt **1**. In non polar solvents (dichloromethane, entry 3), precipitation of metallic palladium is observed during the course of the reaction and **3** is formed in low yield (12 %). The cross-coupling is inhibited in polar solvents such as dimethylsulfoxide (entry 4). Addition of bases, particularly triethylamine (entry 8), results in the reduction of the diazonium salt and toluene is obtained as the major product. The reaction yield decreases upon addition of stabilising phosphine ligand, such as triphenylphosphine (entry 9). Bis(dibenzylideneacetone) palladium(0) (entry 10) or heterogeneous catalyst Pd/C (entry 11) show interesting catalytic activity at 20°C, affording **3** in 78-86% yield. However a longer reaction time is required, even at 40°C, under heterogeneous conditions (entry 11).

Table 1 : Coupling of 4-methylbenzenediazonium fluoroborate with phenylboronic acid[a].



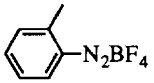
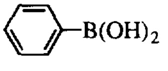
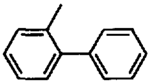
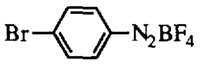
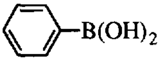
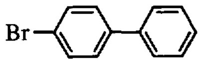
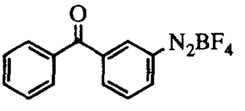
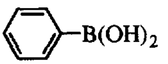
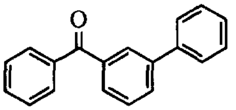
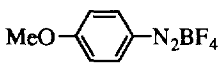
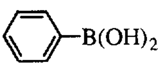
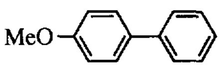
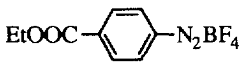
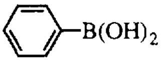
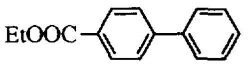
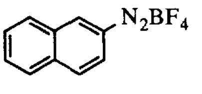
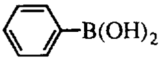
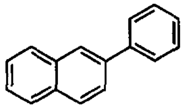
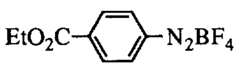
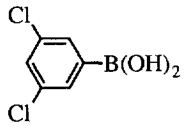
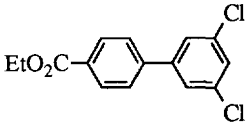
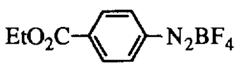
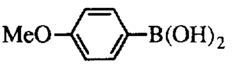
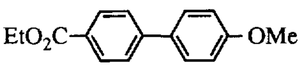
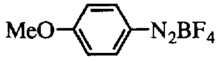
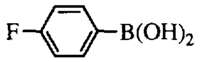
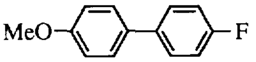
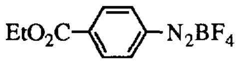
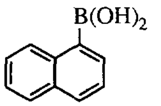
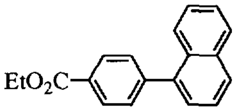
1 **2** **3**

Entry	Catalyst	Solvent	Base[b]	Time (h)	Conversion[c] (%)	Yield[d]
1	$Pd(OAc)_2$	MeOH		0.08	100	49
2	$Pd(OAc)_2$	H_2O		2	100	45
3	$Pd(OAc)_2$	CH_2Cl_2		0.5	15	12
4	$Pd(OAc)_2$	DMSO		24	13	6
5	$Pd(OAc)_2$	Et_2O		24	65	58
6	$Pd(OAc)_2$	THF		1	100	74
7	$Pd(OAc)_2$	1,4-dioxane		4	100	87
8	$Pd(OAc)_2$	1,4-dioxane	Et_3N	1	100	7
9	$Pd(OAc)_2$ / 2 PPh_3	1,4-dioxane		16	100	69
10	$Pd(dba)_2$[e]	1,4-dioxane		32	100	86
11	Pd/C	1,4-dioxane		96	100	78

a. Reactions were carried out at 20°C using 5 mol % of catalyst, arylboronic acid (1.2 mmol), diazonium salt (1 mmol) in 2 ml solvent. b. 2 equivalents of base used. c. Determined by the volume of N_2 given off. d. GLC yields. e. Bis(dibenzylideneacetone) palladium.

The scope of the described coupling was evaluated by investigating the reactivity of a variety of arenediazonium fluoroborates[11,12] and arylboronic acids[13]. As described in Table 2, the cross-coupling reactions[14], conducted at room temperature in dioxane and in the presence of 5% $Pd(OAc)_2$, afford biaryl products in moderate to good yields. The nature of the substituents on the diazonium salt does not seem to affect greatly the reaction yields. Arenediazonium fluoroborate bearing either electron withdrawing functional groups (entries 3,5, 7, 8 and 10) or donating groups (entries 1,4 and 9) react smoothly with various arylboronic acids giving moderate to good yields (57-88 %) of coupled products. Good yield of biaryl can be obtained even when the diazonium salt has a substituent in the ortho position (entry 1). 2-Naphthalenediazonium fluoroborate seems to be less reactive and provides 2-phenylnaphthalene in a moderate 60 % yield on coupling with phenylboronic acid (entry 6). The coupling of 4-bromobenzenediazonium salts with phenylboronic acid, which yields exclusively 4-bromobiphenyl (entry 2), is particularly noteworthy as it can provide a promising way to prepare unsymmetrically disubstituted benzenes by a stepwise double cross-coupling. Interestingly, reaction of 1-naphthylboronic acid with 4-(carboxyethyl)benzenediazonium fluoroborate is comparatively more rapid and affords the coupled product in high yield (entry 10 compared to entry 5).

Table 2 : Coupling of arenediazonium tetrafluoroborates with arylboronic acids[a].

Entry	ArN_2BF_4	$ArB(OH)_2$	Time (h)	Product	Yield[b] (%)
1			4.5		(95)
2			< 24		77[c]
3			4		82
4			5		79
5			2		78
6			32		62
7			< 20		65
8			56		57
9			24		60
10			0.5		88

a. Reactions were carried out at 20°C using 5 mol % of $Pd(OAc)_2$, arylboronic acid (1.2 eq.), diazonium salt (1 to 3 mmol) in 1,4-dioxane (2 ml/mmol). b. Isolated yields. Yields in parenthesis are GLC yields based on ArN_2BF_4. c. Contains 4-5% of biphenyl.

In summary, we have found that arenediazonium tetrafluoroborates are efficient substrates in palladium-catalysed cross-couplings with arylboronic acids which can be conducted under mild conditions and without addition of a base. Moreover, from an industrial view point, arenediazonium tetrafluoroborates, which derive from anilines are economically more advantageous than arylbromides or iodides. Various electron withdrawing or donating functional groups can be present in the structures of both arenediazonium salts and arylboronic acids. The described reaction displays an interesting chemoselectivity due to the high reactivity of arenediazonium salts compared to arylbromides. It represents a promising way to achieve chemoselective double cross-couplings on aromatic rings.

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References and notes

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11. Arenediazonium tetrafluoroborates are prepared according to Roe, A. *Organic Reactions* **1949**, *5*, 193-228 and are purified, several times if necessary, by precipitation of the filtered solution of reagent grade acetone by the addition of diethyl ether. The salts can be stored under an argon atmosphere at -20°C for several months.
12. Use of arenediazonium hexafluorophosphate instead of arenediazonium tetrafluoroborate, affords only small amounts of the expected cross-coupling product.
13. Arylboronic esters are not reactive under the conditions described.
14. General procedure for the preparation of unsymmetrical biaryls : 1 mmol of arenediazonium salt, 1.2 mmol of arylboronic acid and 5 mol% of $Pd(OAc)_2$ were placed in a flask under an argon atmosphere, in the dark. Then, 2 ml of anhydrous and degassed 1,4-dioxane were added and the resulted suspension was stirred at 20°C. The course of the coupling was followed by measuring gas evolution with a gas buret. After completion of the gas evolution, the catalyst was filtered off and washed with diethyl ether. The organic phase was washed with saturated sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was removed and the crude product was purified by chromatography on silica gel.

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