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Cross-Coupling Reactions of Arenediazonium Tetrafluoroborates with Potassium Aryl- or Alkenyltrifluoroborates Catalyzed by Palladium

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Abstract : Potassium aryl- and alkenyltrifluoroborates react smoothly with arenediazonium tetrafluoroborates under mild conditions in the presence of a palladium catalyst and without added base.
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Cross-coupling reactions of organoboron compounds with organic halides and triflates, catalyzed by palladium (Suzuki reaction), have been shown to provide a versatile tool for the selective formation of carbon-carbon bonds[1].

We have recently reported that arenediazonium tetrafluoroborates were effective substrates in the coupling reaction with aryl- and alkenylboronic acids under mild conditions[2] : room temperature, absence of both phosphine and added base (Scheme 1). The described reaction was limited to sterically unhindered organoboronic acids[2b] and by the use of isolable organoboronic acids (boronic ester did not undergo the cross-coupling reaction).

$$\text{Ar-N}_2\text{BF}_4 \quad + \quad \text{R-B(OH)}_2 \xrightarrow[\substack{\text{1,4-dioxane} \\ 20^\circ\text{C}}]{5\%\ \text{Pd(OAc)}_2} \text{Ar-R}$$

Scheme 1

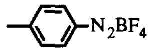
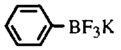
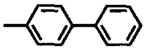
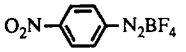
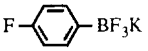
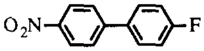
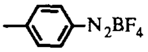
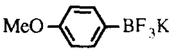
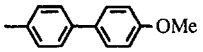
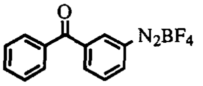
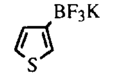
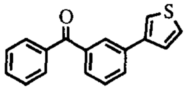
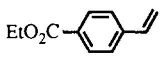
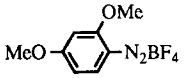
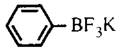
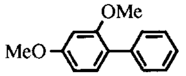
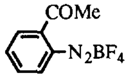
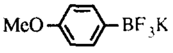
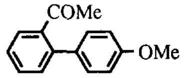
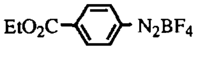
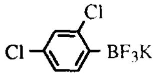
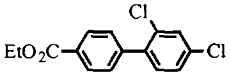
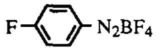
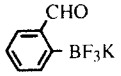
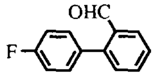
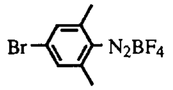
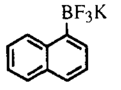
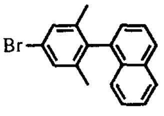
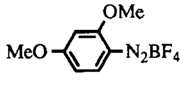
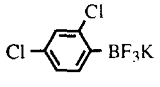
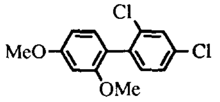
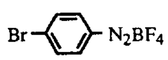
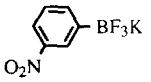
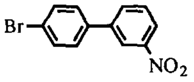
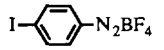
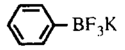
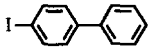
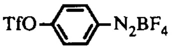
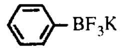
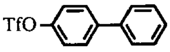
In order to increase the nucleophilicity of the organoborane moiety in the transmetallation step, we thought that isolable organoborates would be good candidates[3]. Recently, Vedejs et al.[4] reported the easy preparation of potassium aryltrifluoroborates (ArBF_3K) from the corresponding boronic acids ; such species being very stable[4,5] , water resistant and easily isolated. We now wish to report that (i) not only potassium alkenyl- and aryltrifluoroborates are suitable as nucleophiles in the palladium-catalyzed cross-coupling reaction with arenediazonium tetrafluoroborates, but (ii) they are much more efficient than the corresponding organoboronic acids (Scheme 2).

$$\underset{\mathbf{1}}{\text{Ar-N}_2\text{BF}_4} \quad + \quad \underset{\mathbf{2}}{\text{R-BF}_3\text{K}} \xrightarrow[20^\circ\text{C}]{\text{cat. [Pd]}} \text{Ar-R}$$

R = alkenyl or aryl.

Scheme 2

Table : Palladium-catalyzed cross-coupling reactions of arenediazonium fluoroborates with potassium aryl- or alkenyltrifluoroborates[a].

Entry	ArN_2BF_4	$Ar'BF_3K$	Conditions[b]	Time (h)	Product	Yield[c]
1			A	3.7		(88) [87]
2			A	2.5		92
3			A B	4 1		(86) (83)
4			A	3		86
5			A	1		65
6			A	6.5		69 [32]
7			A	1.7		96
8			A B	72 1.5		(26) [5] 73
9			B	4		67
10			A B	24 120		21 (10)
11			B	20		traces[d]
12			B	8		60 [34]
13			B	22		41 [17]
14			A	1		66

a) See notes 7 and 9. b) Conditions A : $Pd(OAc)_2$/1,4-dioxane. Conditions B : $Pd_2(\mu\text{-}OAc)_2(P(o\text{-tolyl})_3)_2$/MeOH. c) Isolated yields. Yields in parenthesis are GLC yields based on ArN_2BF_4. Yields in brackets are obtained when using the corresponding organoboronic acid as reagent in the previously described conditions[2]. d) Only 20% conversion.

Indeed, treatment of arenediazonium tetrafluoroborate **1** with potassium aryl- or alkenyltrifluoroborate[6] **2** (Scheme 2) under the conditions previously described for the cross-coupling with organoboronic acids[2], - i. e. at room temperature, in the presence of $Pd(OAc)_2$ in 1,4-dioxane (conditions A[7]) - affords unsymmetrical biaryls containing diverse functionalities as shown in the Table.

Reaction yields are high even when ortho-substituted arenediazonium fluoroborates are involved (entries 6 and 7). Direct comparison clearly show that, under the same reaction conditions (conditions A), potassium aryltrifluoroborates are more efficient than the corresponding arylboronic acids (entries 6, 8, 12, 13).

When potassium aryltrifluoroborates bearing an ortho-substituent are involved (entries 8-11), in the presence of palladium acetate in 1,4-dioxane (conditions A), low yields of biaryls are obtained with a rapid precipitation of metallic palladium. The cross-coupling can be improved by using the palladacycle *trans*-di(μ-acetato)-bis[*o*-(di-*o*-tolylphosphino)benzyl]dipalladium(II)[8] and performing the reaction in methanol (conditions B[9]). These conditions are however inefficient when both the substrates are sterically hindered (entries 10 and 11).

Reactions involving arenediazonium tetrafluoroborates containing an iodide, bromide or triflate substituent are characterised by a high chemoselectivity, leading respectively to biaryls having a halide or triflate functional group[10] (entries 12-14).

Potassium aryl- and alkenyltrifluoroborates can thus be effective reagents in palladium-catalyzed cross-coupling reactions with arenediazonium tetrafluoroborates. The described reaction should be useful in organic synthesis for several reasons. Readily availability of arenediazonium tetrafluoroborates from aromatic amines is superior to the synthesis of the corresponding halides. Potassium aryl- and alkenyltrifluoroborates are more stable and easier to handle than the corresponding organoboronic acids. Moreover, they are more reactive. The higher reactivity of RBF_3K - compared to $RB(OH)_2$ - is very probably due to the higher nucleophilicity of the organic group on boron atom[1,3]. This reaction proceeds under mild conditions tolerating bromide, iodide and triflate substituents. Thus double cross-coupling reactions to introduce two different groups on benzene ring are possible. Synthetic applications are underway in our laboratory.

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6. Potassium organotrifluoroborates were prepared according to ref. 4. To a methanol solution of organoboronic acid was added dropwise, at room temperature, a concentrated aqueous solution of KHF_2 (3.3 equivalents). The resulting suspension was stirred 10 minutes and the solvent was removed in vacuo. The solid was extracted with several portions of acetone and the solvent was removed to afford crude potassium organotrifluoroborate. It was then purified by recristallisation or reprecipitation from acetone/diethyl ether. Yields of purified products were generally over 95%.

   Potassium vinyltrifluoroborate was prepared analogously from the commercially available 4,4,6-trimethyl-2-vinyl-1,3,2-dioxaborinane (Acros Organics).

7. General procedure (conditions A) : arenediazonium tetrafluoroborate (1 mmol), potassium aryl- or alkenyltrifluoroborate (1.2 mmol) and $Pd(OAc)_2$ (5 mol%) were mixed under an argon atmosphere, in a foil covered flask. Anhydrous 1,4-dioxane (4 ml) was then added and the resulting suspension stirred at 20°C for the indicated time. The course of the reaction was followed by measuring gas evolution with a gas buret. After completion, the reaction mixture was diluted with diethyl ether, washed several times with brine and dried over anhydrous magnesium sulphate. The solvent was then removed and the crude product purified by column chromatography on silica gel.

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9. General procedure (conditions B) : the same procedure as that described in reference 7 was employed, except that $Pd(OAc)_2$ and 1,4-dioxane were respectively replaced by $Pd_2(\mu\text{-}OAc)_2(P(o\text{-tolyl})_3)_2$ and methanol.

   Spectroscopic data for selected biaryl compounds :

   3-(3-thienyl)-1-benzoylbenzene (entry 4) : mp 51.5-52.5°C, light yellow solid ; ^1H NMR (200 MHz, $CDCl_3$, ppm) ∂ 8.06 (1H, td, J = 1.7 and 0.4 Hz), 7.86 (2H, d, J = 6.8 Hz), 7.83 (1H, ddd, J = 7.6, 1.9 and 1.2 Hz), 7.71 (1H, ddd, J = 7.7, 1.7 and 1.3 Hz), 7.58-7.66 (1H, m), 7.47-7.56 (4H, m), 7.43 (1H, s), 7.42 (1H, d, J = 0.7 Hz) ; ^{13}C NMR (50 MHz, $CDCl_3$, ppm) ∂ 196.5, 141.2, 138.1, 137.5, 136.0, 132.5, 130.2, 130.0, 128.7, 128.3, 127.7, 126.5, 126.1, 121.1.

   2-(4-fluorophenyl)benzaldehyde (entry 9) : oil ; ^1H NMR (200 MHz, $CDCl_3$, ppm) ∂ 10.0 (1H, s), 8.03 (1H, dd, J = 7.6 and 1.3 Hz), 7.65 (1H, td, J = 7.5 and 1.5), 7.50 (1H, t, J = 7.3 Hz), 7.41 (1H, d, J = 7.4 Hz), 7.36 (2H, dd, $^3J_{HH}$ = 8.8, $^4J_{HF}$ = 5.4 Hz), 7.17 (2H, t, $^3J_{HH}$ = $^3J_{HF}$ = 8.7 Hz) ; ^{13}C NMR (50 MHz, $CDCl_3$, ppm) ∂ 192.1, 162.9 (d, J_{CF} = 247 Hz), 144.8, 133.8, 133.7, 131.7 (d, J_{CF} = 8.2 Hz), 130.9, 128.0, 127.9, 115.5 (d, J_{CF} = 22 Hz).

10. In the case of 4-iodobenzenediazonium tetrafluoroborate, an analysis (GC/MS, column DB-1701, J&W Scientific) of the crude product revealed the presence of 4-5% of [1,1';4',1'']terphenyl.

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