

Microwave enhanced ligand- and base-free cross-coupling of potassium aryltrifluoroborates salts with aryl triflates

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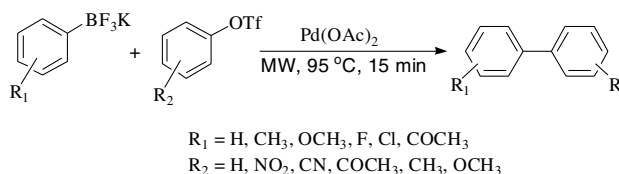
Abstract—A microwave enhanced ligand- and base-free protocol for the cross-coupling of potassium aryltrifluoroborate salts with triflates is reported.

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The Suzuki–Miyaura cross-coupling reaction is one of the most versatile and commonly utilized methods for the selective construction of carbon–carbon bonds.¹ The reaction provides a convenient pathway to a range of pharmaceuticals, herbicides, natural products, polymers, and liquid crystalline materials.² Generally, boronic acids or esters are used in these palladium catalyzed reactions. Recently potassium organotrifluoroborate salts have been reported to be effective Suzuki–Miyaura reagents, exhibiting several advantages over trivalent organoboronic acids and esters. These include air and water stability, ease of preparation and purification, and generally higher reactivity.³

The use of microwaves in organic reactions has attracted considerable attention in recent years. Microwaves shorten reaction times, enhance reaction rates, and improve product yields.⁴ In this letter, we report a protocol for the syntheses of biaryl products utilizing the palladium catalyzed cross-coupling of potassium organotrifluoroborates with aryl triflates in aqueous ethanol in the absence of a base or ligand under microwave irradiation. The desired products were obtained in good to excellent yields within 15 min, whereas the same reactions required several hours under thermal conditions.⁵ The optimized reaction conditions utilize a catalyst loading of 1.2 mol % of Pd(OAc)₂. In the absence of the palladium catalyst, no reaction occurs (Scheme 1).

The scope of the reaction was investigated by coupling potassium *p*-tolyltrifluoroborates with electronically diverse aryl triflates (Table 1). Aryl triflates containing

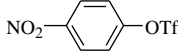
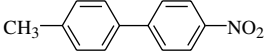

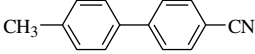
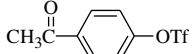
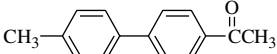
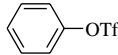
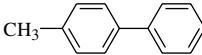
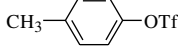
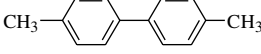
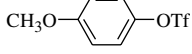
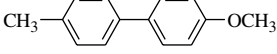


Scheme 1.

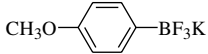
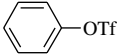
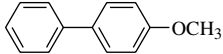
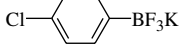
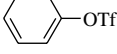
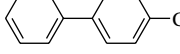

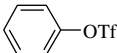
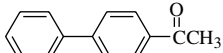
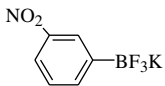
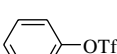
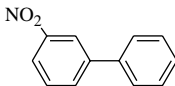
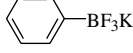
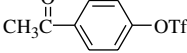
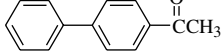
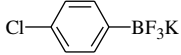
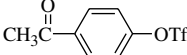
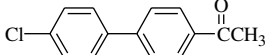
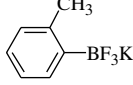
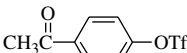
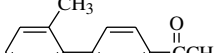
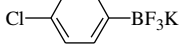
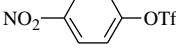
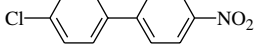
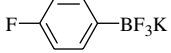

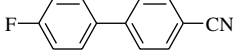
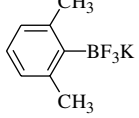

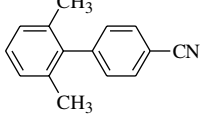
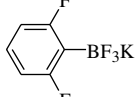

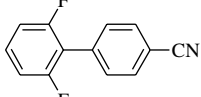
electron withdrawing groups (Table 1, entries 1–3), electron donating groups (Table 1, entries 5 and 6), and electronically neutral groups (Table 1, entry 4) were successfully coupled with potassium *p*-tolyltrifluoroborate to produce the corresponding products in good yields. In a recent report by Molander, ligand-free Suzuki–Miyaura coupling reactions were found to be applicable only to electron-deficient aryl triflates.⁶ Only traces of product were isolated from cross-coupling reactions of electron rich aryl triflates such as *p*-methoxyphenyl triflate.⁷ Other aryltrifluoroborate salts were also investigated in the coupling reaction (Table 2). Excellent yields were achieved in nearly all cases. Potassium aryl trifluoroborates bearing electron withdrawing (entries 2, 3, 4, 6, 8, 9, and 11), electron neutral (entry 5), and electron donating (entries 1, 7 and 10) groups all reacted with the aryl triflates to produce the desired products in good yields. Steric hindrance appears to have little impact on the cross-coupling reaction. For instance, coupling products were obtained from *ortho*-substituted substrates in moderate yields. Even in the case of highly hindered 2,6-dimethylphenyltrifluoroborate, the desired product was obtained in a 61% yield. Notably, the reaction conditions are mild and tolerate a variety of functionality such as ketones, nitriles, halide and nitro groups.

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Table 1. Microwave enhanced cross-coupling reactions of potassium *p*-tolyltrifluoroborate with aryl triflate

Entry	Aryl triflate	Coupling product ^a	Yield% ^b
1			88
2			85
3			94
4			92
5			63
6			61

^a All products were identified by ¹H, ¹³C NMR, and by comparison with authentic samples.^b Isolated yields.**Table 2.** Microwave enhanced cross-coupling reactions (Scheme 1)

Entry	Aryltrifluoroborate	Aryltriflate	Coupling product ^a	Yield% ^b
1				95
2				98
3				60
4				50
5				90
6				89
7				85
8				86
9				99
10				56
11				51

^a All products were identified by ¹H NMR, ¹³C NMR, and by comparison with authentic samples.^b Isolated yields.

Aryl triflates are base sensitive and thermally liable so that long reaction times and basic conditions lead to their destruction.⁸ The current protocol using microwave irradiation in the absence of base eliminates these shortcomings.

The synthesis of 4-methylbiphenyl (Table 1, entry 1) is representative. Potassium *p*-tolyltrifluoroborate (108 mg, 0.55 mmol), phenyltriflate (113 mg, 0.50 mmol), and Pd(OAc)₂ (1.40 mg, 0.60 mol %) are dissolved in aqueous ethanol (1:1 by volume 5 mL). The resultant mixture is placed in the microwave cavity of a CEM discover microwave unit and allowed to react at 95 °C for 15 min. The reaction mixture is diluted with water (5 mL) extracted with ethyl acetate (3 × 10 mL), and the organic phase separated. After drying over anhydrous sodium sulfate, the solution is concentrated, and the mixture chromatographed over silica gel column using hexane-ethyl acetate (50:1) as eluent to yield a white solid (77 mg, 92% yield).

In conclusion, the palladium catalyzed cross-coupling reaction of potassium aryltrifluoroborates with aryl triflates is enhanced through the use of microwave irradiation. The advantages of the microwave protocol include short reaction times, fewer side reactions, and higher product yields, when compared to conventional Suzuki–Miyaura cross-coupling reaction.

Acknowledgements

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