

Microwave enhanced cross-coupling reactions involving potassium organotrifluoroborates

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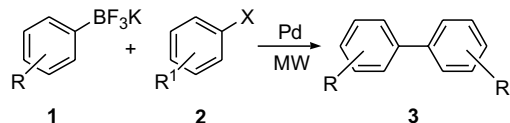
Abstract—Palladium catalyzed coupling reactions of potassium aryltrifluoroborates with aryl iodides occur rapidly utilizing microwave irradiation. The coupled products are produced in excellent yields.

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The palladium catalyzed cross-coupling reaction between organoboron compounds and organic halides provides a powerful tool for the formation of carbon–carbon bonds.¹ Recently, the utility of potassium organotrifluoroborates as intermediates for the synthesis of biaryl compounds has become widely recognized.^{2,3} Both their straightforward preparation and chemical reactivity add to the versatility of potassium organotrifluoroborates in organic synthesis. For example, reactions of trifluoroborate reagents are unaffected by water. They also proceed in a highly regio- and stereo-selective manner. The reaction products are readily isolated from the inorganic byproducts of the reaction.


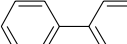

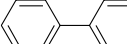
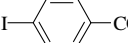
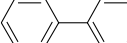
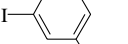
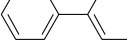
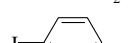
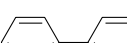
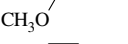
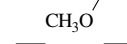
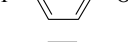

The use of microwaves in organic synthesis has also gained importance.⁴ Microwave systems provide the opportunity to complete complex reactions in minutes. In this letter, we report the use of microwaves in coupling reactions⁵ involving potassium organotrifluoroborates. We have found that palladium catalyzed coupling reactions of potassium aryltrifluoroborates with aryl iodides furnish the desired products within 10 min in excellent yields whereas the same reactions require several hours under thermal conditions (Scheme 1).

To evaluate the new procedure,⁶ potassium phenyltrifluoroborate was allowed to react with various substituted iodobenzenes (Table 1). A catalyst loading of 2 mol % PdCl₂(dppf)CH₂Cl₂ with 3.0 equiv of Hunig's



Scheme 1.

Table 1. Microwave enhanced cross-coupling reactions of potassium phenyltrifluoroborate with aryl iodides (Scheme 1)^a

Entry	Aryl iodide 2	Coupling product 3	Yields ^b (%)
1			98
2			84
3			93
4			98
5			100
6			100
7			77

^a All reactions were run at 100 °C for 10 min.

^b Isolated yields.

Keywords: Suzuki coupling; Trifluoroborates; Microwave; Organoboron.

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Table 2. Microwave enhanced cross-coupling reactions (Scheme 1)^a

ArBF ₃ K, 1	Aryl iodide, 2	Coupling product, 3	Yields ^b (%)
			98
			92
			98
			96
			85
			86
			94
			50

^a All reactions were run in ⁱPrOH–H₂O (2:1) at 100 °C for 10 min.^b Isolated yields.

base (*i*-Pr₂NEt) in an isopropanol–water mixture (2:1) was found to provide the coupled products in good to excellent yields. In the absence of a palladium catalyst, no coupling product was observed. The synthesis of 4-chlorobiphenyl is representative of the procedure utilized (Table 1, entry 1). A dry Pyrex tube fitted with an air-tight rubber cap was charged with potassium phenyltrifluoroborate (92.0 mg, 0.50 mmol), 1-chloro-4-iodobenzene (121.0 mg, 0.50 mmol), and PdCl₂(dppf)·CH₂Cl₂ (9.0 mg, 0.01 mmol). Under argon, Hunig's base (0.26 mL, 1.50 mmol) and argon-purged isopropanol–water (2:1, 5.0 mL) were then added. The resulting mixture was placed in a CEM microwave unit and allowed to react at 100 °C for 10 min. The reaction mixture was transferred to a separatory funnel and diluted with ethyl ether and water. The organic phase was separated and dried over anhydrous sodium sulfate. The ether solution was filtered and the filtrate concentrated prior to silica gel chromatography using hexane–ethyl acetate (50:1). The fractions were concentrated and dried in vacuo to give 92.0 mg of pure 4-chlorobiphenyl (98%) as a white solid. The reaction was insensitive to the nature of the substituents on the aromatic ring. Reagents containing electron withdrawing groups (Table 1, entries 1–4), electron donating groups (Table 1, entries 5 and 6) and sterically bulky substituents (Table 1, entry 7) all provided coupling products in excellent yields. Having successfully demonstrated the use of microwaves to enhance the Suzuki coupling of potassium phenyltrifluoroborate

with various aryl halides, we then investigated the use of other substituted potassium aryltrifluoroborates in the coupling reaction (Table 2). Essentially all reagents provided the cross-coupling products in excellent yields.⁷

In conclusion, the microwave enhanced cross-coupling reaction of potassium aryltrifluoroborates with substituted iodobenzenes provides an excellent route to highly functionalized biaryl reagents.

Acknowledgements

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References and notes

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7. Analytical data for new compounds: 4'-Fluoro-4-trifluoromethoxy-biphenyl: ^1H NMR (CDCl_3 , 300 MHz): δ 7.53–7.46 (m, 4H, $-\text{C}_6\text{H}_4$), 7.28–7.08 (m, 4H, $-\text{C}_6\text{H}_4$). ^{13}C NMR (CDCl_3 , 75.5 MHz): δ 164.2, 160.9, 138.9, 128.7, 128.6, 128.4, 128.3, 121.2, 115.9, 115.6. ^{19}F NMR (CDCl_3 , 282.3 MHz): δ –58.2, –115.4. Calcd for $\text{C}_{13}\text{H}_8\text{OF}_4$: C, 60.95; H, 3.15. Found: C, 61.52; H, 3.14. 4'-Chloro-4-trifluoromethoxy-biphenyl: ^1H NMR (CDCl_3 , 300 MHz): δ 7.55–7.26 (m, 8H, $2 \times -\text{C}_6\text{H}_4$); ^{19}F NMR (CDCl_3 , 282.3 MHz): δ –62.8. Calcd for $\text{C}_{13}\text{H}_8\text{OF}_3\text{Cl}$: C, 57.27; H, 2.96. Found: C, 57.64; H, 2.91. 2-Methyl-4'-trifluoromethoxy-biphenyl. ^1H NMR (CDCl_3 , 300 MHz): δ 7.34–7.18 (m, 8H, $2 \times -\text{C}_6\text{H}_4$), 2.25 (s, 3H, $-\text{CH}_3$). ^{19}F NMR (CDCl_3 , 282.3 MHz): δ –58.1. Calcd for $\text{C}_{14}\text{H}_{11}\text{OF}_3$: C, 66.67; H, 4.40. Found: C, 66.78; H, 4.44. 2-Methoxy-4'-trifluoromethoxy-biphenyl. ^1H NMR (CDCl_3 , 300 MHz): δ 7.56–6.96 (m, 8H, $2 \times -\text{C}_6\text{H}_4$), 3.79 (s, 3H, $-\text{OCH}_3$); ^{13}C NMR (CDCl_3 , 75.5 MHz): δ 170.6, 156.3, 137.1, 130.8, 130.7, 129.1, 129.0, 120.8, 120.4, 111.1, 55.4; ^{19}F NMR (CDCl_3 , 282.3 MHz): δ –58.0. Calcd for $\text{C}_{14}\text{H}_{11}\text{O}_2\text{F}_3$: C, 62.69; H, 4.13. Found: C, 62.64; H, 4.11. 2,4,6-4'-Tetrafluoro-biphenyl: ^1H NMR (CDCl_3 , 300 MHz): δ 7.37 (m, 2H), 7.13 (m, 2H), 6.74 (m, 2H). ^{19}F NMR (CDCl_3 , 282.3 MHz): δ –109.1, –111.9, –113.5. Calcd for $\text{C}_{12}\text{H}_6\text{F}_4$: C, 63.73; H, 2.67. Found: C, 64.91; H, 2.80.