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Microwave enhanced cross-coupling reactions involving alkenyl- and alkynyltrifluoroborates

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Abstract—Cross-coupling reactions of potassium arylvinyltrifluoroborates with aryl iodides in the presence of a palladium catalyst occur rapidly utilizing microwave irradiation. The coupled products are produced in excellent yields. Alkynyltrifluoroborates also undergo the coupling reaction.

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It has been well documented that palladium catalyzed cross-coupling reactions between organoboron compounds and organic halides (as well as triflates) are powerful tools for the formation of carbon–carbon bonds.¹ There are, however, problems specific to alkenylboronic acids and esters in the Suzuki-Miyaura coupling reactions. For example, vinylboronic acids can be lost to polymerization. Furthermore, vinylboronic esters are not always selective in cross-coupling reactions, yielding mixtures of Suzuki-Miyaura and Heck coupled products.² Recent studies have revealed that potassium alkenyltrifluoroborates and alkynyltrifluoroborates offer solutions to a number of problems that occur in organoboron coupling reactions.³ We have begun to explore the use of microwave irradiation as an alternative to thermal heating in reactions using potassium organotrifluoroborates. The use of microwaves in organic synthesis has gained importance in organic chemistry in recent years.⁴ We recently reported the first use of microwaves in cross-coupling reactions involving potassium aryltrifluoroborates.⁵ In the course of those studies, we developed a microwave assisted, palladium catalyzed cross-coupling reaction of potassium vinyltrifluoroborates with aryl halides. In this letter, we report the results of this study, coupling reactions that can be used to prepare a variety of stilbenes in excellent yields in less than ten minutes (Scheme 1).

The photochemistry and physics of stilbenes have been the subject of numerous investigations. In medicine, stilbene derivatives have proven to be antioxidants.⁶ They also have important applications in macromolecular chemistry and nanoscience.⁷

The scope of the reaction was investigated by allowing potassium phenylvinyltrifluoroborate, 1, to react with various substituted iodobenzenes (Table 1). A catalyst loading of $2 \mod \% \text{PdCl}_2(\text{dppf})\text{CH}_2\text{Cl}_2$, along with



Scheme 1.

Keywords: Alkenyltrifluoroborates; Alkynyltrifluoroborates; Microwave irradiation.

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Entry	Aryl iodide, 2	Product, 3	Yield (%)
1	I 2a	Ph 3a	67
2	F 2b	Ph F 3b	61
3	Cl 2c	Ph Cl 3c	99
4	COCH ₃ 2d	Ph COCH ₃ 3d	91
5	2e I NO ₂	Ph NO ₂	76
6	2f OCH ₃	Ph OCH ₃ 3f	79
7	CH ₃ CH ₃	Ph CH ₃ CH ₃	96
8	I CH ₃ 2h	Ph CH ₃ 3h	92

^a All yields are of pure products isolated by silica gel chromatography.

3.0 equiv of Hünig's base (*i*-Pr₂NEt), in isopropanol/ water (2:1) was found to provide the coupled products in good to excellent yields.⁸ In the absence of a palladium catalyst, no coupling product was observed. The reactions are very straightforward stereoselective and relatively insensitive to the nature of the substituents. Reagents containing electron withdrawing groups (Table 1, entries 2-5), electron donating groups (Table 1, entries 6-8) all provide the cross-coupled styrene products in high yields. Having successfully utilized microwaves to enhance Suzuki coupling of potassium trans-2-phenylvinyltrifluoroborate with aryl halides, we then investigated the use of other substituted potassium arylvinyltrifluoroborates (Table 2). All reactants provided the cross-coupled stilbene products in excellent yields (Table 2, entries 1-6). An aliphatic vinyltrifluoroborate also readily participated in the reaction (Table 2, entry 7). Yields were generally somewhat lower for coupling reactions involving the alkynyl trifluoroborates; a situation also noted in thermal coupling reactions^{3f} (Table 2, entries 8–13).

The reactions are rapid and simple to perform. In a typical experiment, the organotrifluoroborate⁹ (0.50 mmol) and palladium catalyst (0.01 mmol) are placed in an argon flushed pyrex tube. The aryl halide (0.50 mmol) is then added along with diisopropyl ethyl amine (1.5 mmol) and 5 mL of isopropanol/water (2:1). The pyrex tube is capped with a rubber septum and placed in a CEM microwave unit and allowed to react at 100 °C for 10 min. The product is worked up by adding water (15 mL) and ether (15 mL), the ether layer separated, the solvent extracted, and the product isolated by column chromatography. The product yields generally exceed those obtained in the thermal reactions by ~10%³ⁱ whereas the coupling yields are similar for thermal reactions generating alkyne products.^{3j,k}

Table 2. Microwave enhanced cross-coupling reactions for the synthesis of styrenes and enynes^a

Entry	R BF ₃ K	Aryl iodide	Product ^b	Yields (%)
1	CF3		CT CT CT	92
2	CF3	I NO ₂		81
3	CF3	I COCH3	CE.	95
4	CI BF ₃ K	I NO2		87
5	CI BF3K	I OCH3	CI OCH3	85

 Table 1. Microwave enhanced cross-coupling reaction of potassium

 trans-2-phenylvinyltrifluoroorate, 1 with iodobenzenes^a

Table 2 (continued)

Entry	R BF ₃ K	Aryl iodide	Product ^b	Yields (%)
6	CH ₃ BF ₃ K	I CI	CH	94
7	C ₇ H ₁₅ BF ₃ K	F	C ₇ H ₁₅	91
8	BF ₃ K	F	✓————————————————————————————————————	60
9	CH ₃ -BF ₃ K	I CI	CH ₃ -Cl	65
10	CH ₃ O-	I CI	сн,о-	68
11	CH ₃ O-BF ₃ K	I Br	CH ₃ O — Br	72
12	CH ₃ O-BF ₃ K		сн,о-	69
13	NCBF ₃ K	I		52

^a All yields are of pure products isolated by silica gel chromatography.

^b Satisfactory combustion analyses were obtained for all new compounds.¹⁰

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References and notes

- (a) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. J. Am. Chem. Soc. 2005, 127, 4685; (b) Littke, A. F.; Fu, G. C. Angew. Chem., Int. Ed. 2002, 41, 4176; (c) Suzuki, A. J. Organomet. Chem. 1999, 576, 147; (d) Miyaura, N.; Suzuki, A. Chem. Rev. 1995, 95, 2457; (e) Suzuki, A. In Metal-Catalyzed Cross-Coupling Reactions; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998, Chapter 2; (f) Miyaura, N.; Yamada, K.; Suzuki, A. Tetrahedron Lett. 1979, 36, 3437.
- (a) Lightfoot, A. P.; Maw, G.; Thirsk, C.; Twiddle, S.; Whiting, A. *Tetrahedron Lett.* **2003**, *44*, 7645; (b) Hunt, A. R.; Stewart, S. K.; Whiting, A. *Tetrahedron Lett.* **1993**, *34*, 3599.
- (a) Molander, G. A.; Felix, L. A. J. Org. Chem. 2005, 70, 3950; (b) Tremblay-Morin, J.-P.; Raeppel, S.; Gaudette,

F. Tetrahedron Lett. 2004, 45, 3471; (c) Molander, G. A.; Ribagorda, M. J. Am. Chem. Soc. 2003, 125, 11148; (d) Quach, T. D.; Batey, R. A. Org. Lett. 2003, 5, 1381; (e) Molander, G. A.; Bernardi, C. R. J. Org. Chem. 2002, 67, 8424; (f) Molander, G. A.; Katona, B. W.; Machrouhi, F. J. Org. Chem. 2002, 67, 8416; (g) Pucheault, M.; Darses, S.; Genet, J.-P. Eur. J. Org. Chem. 2002, 3552; (h) Molander, G. A.; Rivero, M. R. Org. Lett. 2002, 4, 107; (i) Batey, R. A.; Thadani, A. N.; Smil, D. V.; Lough, A. Synthesis 2000, 990; (j) Darses, S.; Michauld, G.; Genet, J.-P. Eur. J. Org. Chem. 1999, 1875; (k) Stefani, H. A.; Cella, R.; Dorr, F. A.; Pereira, C. M.; Zeni, G.; Fome, L. Tetrahedron Lett. 2005, 46, 563.

 For microwave assisted coupling reactions see: (a) Liu, Y.; Khemtong, C.; Hu, J. Chem. Commun. 2004, 398; (b) Wang, Y.; Sauer, D. R. Org. Lett. 2004, 6, 2793; (c) Solodenko, W.; Schoen, U.; Messinger, J.; Glinschert, A.; Kirschning, A. Synlett 2004, 1699; (d) Kappe, C. O. Angew. Chem., Int. Ed. 2004, 43, 6250; (e) Gong, Y.; He, W. Org. Lett. 2002, 4, 3803; (f) Villemin, D.; Gomez-Escalonilla, M. J.; Saint-Clair, J. F. Tetrahedron Lett. 2001, 42, 635; (g) Larhed, M.; Lindeberg, G.; Hallberg, A. Tetrahedron Lett. 1996, 37, 8219.

- 5. Kabalka, G. W.; Al-Masum, M. Tetrahedron Lett. 2005, 46, 6329.
- (a) Merillon, J.-M.; Fauconnean, B.; Teguo, P. W.; Barrier, L.; Vercauteren, J.; Huguet, F. *Clin. Chem.* **1997**, *43*, 1092; (b) Waffo, T. P.; Decendit, A.; Krisa, S.; Deffieux, G.; Vercauteren, J.; Merillon, J.-M. J. Nat. Prod. **1996**, *59*, 1189.
- (a) Andres, P. R.; Lunkwitz, R.; Pabst, G. R.; Bohn, K.; Wounters, D.; Schmatloch, S.; Schubert, U. S. *Eur. J. Org. Chem.* 2003, 3769; (b) Meier, H.; Holst, H. C. *Adv. Synth. Catal.* 2003, 345, 1005.
- Pd₂dba₃·CHCl₃/dppf, Pd₂dba₃/(*o*-toyl)₃, Pd(OAc)₂/dppf, and Pd (OAc)₂ were found to be less effective. Bases evaluated included diisopropylamine, cesium carbonate, potassium carbonate, and triethylamine.
- The trifluoroborates were prepared according to the literature procedures. See, for example: Vedejs, E.; Chapma, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. J. Org. Chem. 1995, 60, 3020, and Ref. 3f.
- 10. Analytical data for new compounds: 4'-Chloro-4-trifluoromethyl-*trans*-stilbene: ¹H NMR (CDCl₃, 300 MHz): δ 7.56 (m, 4H, -C₆H₄), 7.43 (d, J = 8.7 Hz, 2H, -C₆H₄), 7.31 (d, J = 8.7 Hz, 2H, -C₆H₄), 7.05 (m, 2H). ¹³C NMR (CDCl₃, 75.5 MHz): δ 140.3, 135.0, 133.8, 129.7, 128.9, 127.6, 125.6. ¹⁹F NMR (CDCl₃, 282.3 MHz): δ -62.8. Calcd for C₁₅H₁₀F₃Cl: C, 63.73; H, 3.57. Found: C, 63.84; H, 3.53. 4'-Acetyl-4-trifluoromethyl-*trans*-stilbene: ¹H NMR (CDCl₃, 300 MHz): δ 7.97 (m, 2H), 7.61 (m, 6H), 7.21 (s, 2H), 2.61 (s, 3H). Calcd for C₁₇H₁₃OF₃: C, 70.34; H, 4.51. Found: C, 70.31; H, 4.45. 1-Fluoro-4-non-1enylbenzene: ¹H NMR (CDCl₃, 300 MHz): δ 7.25 (m, 2H), 6.96 (m, 2H), 6.32 (d, J = 15.9 Hz, 1H), 6.13 (dt, J = 15.9, 6.9 Hz, 1H), 2.18 (q, J = 7.2 Hz, 2H), 1.47–1.25 (m, 10H), 0.88 (t, J = 6.9 Hz, 3H). ¹³C NMR (CDCl₃, 75.5 MHz): δ 163.4, 134.0, 130.9, 128.4, 127.2, 115.3, 32.9, 31.8, 29.7, 29.3, 22.6, 14.1. Calcd for C₁₅H₂₁F: C, 81.77; H, 9.61. Found: C, 81.21; H, 9.94.