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Palladium(0)-Catalyzed Suzuki−Miyaura Cross-Coupling Reactions of Potassium Aryl- and Heteroaryltrifluoroborates with Alkenyl Bromides

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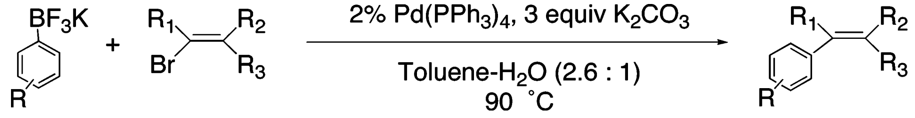

Efficient palladium(0)-catalyzed Suzuki−Miyaura cross-couplings are described. The reactions involving potassium aryl- and heteroaryltrifluoroborates with alkenyl bromides can generally be carried out using $\leq$2 mol % of palladium catalyst and 3 equiv of base in toluene/H$_2$O. When stereodefined alkenyl bromides are employed, the resulting styrene derivatives are accessed stereospecifically. A variety of functional groups are tolerated in both coupling partners.

Introduction

The Suzuki−Miyaura reaction is one of the mildest methods known for metal-mediated carbon−carbon bond formation.[1] This reaction, involving organoboron compounds, presents many significant advantages over other protocols for similar cross-couplings. For example, most organoborons can be prepared easily via transmetalation or hydroboration, and they have a tolerance for a broad range of functional groups. Additionally, the inorganic boron-containing byproducts are less toxic than those of organostannanes used in Stille coupling,[2] and they can be readily removed by a simple workup procedure. By contrast, the complete removal of tin-containing byproducts is a well-recognized problem, and the presence of even traces of these compounds in organic products must be avoided if possible.

Although considerable efforts have been made to develop metal−ligand catalyst systems that facilitate the Suzuki coupling and increase its scope,[3] surprisingly little research has been performed on the nature of the organoboron moiety itself. Boronic acids and boronate esters are the most commonly used derivatives in the Suzuki−Miyaura cross-coupling reactions. However, these are not without their limitations. Boronic acids are subject to cyclic trimerization with loss of water, giving anhydrides (boroxines). This creates difficulties in their direct purification and in the determination of the proper stoichiometry for coupling. Moreover, many boronic acids are prone to protodeborination[4] or homocoupling in the Suzuki process.[5]

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(1) For reviews, see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483. (b) Tsuji, J. *Palladium Reagents and Catalysis*; Wiley and Sons: Chichester, U.K., 1995. (c) Suzuki, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; VCH: Weinheim, Germany, 1998; pp 49−97. (d) Suzuki, A. *J. Organomet. Chem.* **1999**, *567*, 147−168. (e) Suzuki, A. *J. Organomet. Chem.* **2002**, *653*, 83−90. (f) Kotha, S.; Lahiri, K.; Dhurke, K. *Tetrahedron* **2002**, *58*, 9633−9695. (g) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359−1469. (h) Suzuki, A.; Brown, H. C. *Organic Syntheses via Boranes*; Aldrich Chemical Co., Inc.: Milwaukee, WI, 2003; Vol. 3. (i) Miyaura, N., Ed. *Cross-Coupling Reactions*; Springer-Verlag: Berlin, 2002.

(2) (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508−524. (b) Farina, V.; Krishnamurthy, V.; Scott, W. J. *Org. React.* **1997**, *50*, 1−652. For discussions concerning the toxicity of organotin compounds, see: (c) De Mora, S. J. *Tributyltin: Case Study of an Environmental Contaminant*; Cambridge University Press: New York, 1996. (d) Boyer, I. J. *Toxicology* **1989**, *55*, 253−298.

(3) (a) Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722−9723. (b) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550−9561. (c) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020−4028. (d) Bedford, R. B.; Cazin, C. S. J. *Chem. Commun.* **2001**, 1540−1541. (e) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1999**, *37*, 3387−3388. (f) Zhang, C.; Huang, J.; Trudell, M. L.; Nolan, S. P. *J. Org. Chem.* **1999**, *64*, 3804−3805. (g) Netherton, M. R.; Dai, C.; Neuschutz, K.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 10099−10100. (h) Kirchoff, J. H.; Dai, C.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 1945−1947. (i) Gstottmayr, C. W. K.; Bohm, V. P. W.; Herdtweck, F.; Grosche, M.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1363−1365. (j) Botella, L.; Nájera, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 179−181. (k) Kirchhoff, J. H.; Netherton, M. R.; Hills, I. D.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 13662−13663. (l) Kabalka, G. W.; Pagni, R. M.; Hair, C. M. *Org. Lett.* **1999**, *1*, 1423−1425. (m) Kabalka, G. W.; Namboodiri, V.; Wang, L. *Chem. Commun.* **2001**, 775. (n) LeBlond, C. R.; Andrews, A. T.; Sowa, J. R., Jr.; Sun, Y. *Org. Lett.* **2001**, *3*, 1555−1557. (o) Sakurai, H.; Tsukuda, T.; Hirao, T. *J. Org. Chem.* **2002**, *67*, 2721−2722. (p) Grasa, G. A.; Viciu, M. S.; Huang, J.; Zhang, C.; Trudell, M. L.; Nolan, S. P. *Organometallics* **2002**, *21*, 2866−2873 and references therein. (q) Bei, X.; Turner, H. W.; Weinberg, W. H.; Guram, A. S.; Petersen, J. L. *J. Org. Chem.* **1999**, *64*, 6797−6803. (r) Yin, J.; Rainka, M. P.; Zhang, X.-X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1162−1163. (s) Parrish, C. A.; Buchwald, S. L. *J. Org. Chem.* **2001**, *66*, 3820−3827. (t) Feuerstein, M.; Berthiol, F.; Doucet, H.; Santinelli, M. *Synlett* **2002**, 1807−1810 and references therein.

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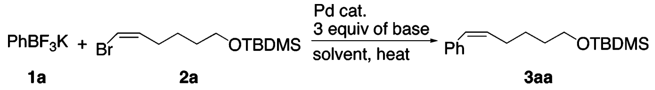
TABLE 1. Optimizing the Cross-Coupling Reaction of Phenyltrifluoroborate with an Alkenyl Bromide



entry	catalyst/ligand	solvent	time	temp	base	% yield[a]
1	5 mol % of $Pd(OAc)_2$/10 mol % of PPh_3	THF/H_2O (10:1)	19 h	70 °C	Cs_2CO_3	43[b]
2	1.2 mol % of $Pd(PPh_3)_4$	THF/H_2O (10:1)	6 h	70 °C	Cs_2CO_3	51[b]
3	1.2 mol % of $Pd(PPh_3)_4$	Tol/H_2O (10:1)	5 h	90 °C	Cs_2CO_3	92[c]
4	1.2 mol % of $Pd(PPh_3)_4$	Tol/H_2O (10:1)	7 h	90 °C		
5	2 mol % of $Pd(PPh_3)_4$	Tol/H_2O (2.6:1)	35 min	90 °C	Cs_2CO_3	97[c]

[a] The reaction was carried out under inert atmosphere (N_2), with degassed solvents. The reactions were performed at concentrations of approximately 0.3 M in organic halide. [b] ^1H NMR yield. [c] Isolated yield.

Boronate esters, even though they perform better from this point of view, lack atom economy. In fact, the diols utilized to create them (e.g., catechol or pinacol) add considerable expense to the overall process and, additionally, must be separated from the coupled products.

Organotrifluoroborates are unique compounds that have been shown to overcome many of the limitations inherent in other organoboron coupling partners. Indeed, it has previously been revealed that potassium organotrifluoroborates provide solutions to many of these problems and restrictions, and a variety of cross-coupling protocols have been revealed.[6] Potassium organotrifluoroborates are easily prepared on large scale (>100 g) from boronic acids or boronate esters by treatment with an aqueous solution of KHF_2 (eq 1),[7] which, on a molar basis, is half the price of catechol and 25 times less expensive than pinacol.

$$ArB(OH)_2 \xrightarrow[\text{solvent, } H_2O \text{, rt}]{3 \text{ equiv of } KHF_2} ArBF_3K \tag{1}$$

The organotrifluoroborates thus generated are monomeric, crystalline solids that can be stored on the shelf indefinitely. Many (>50) are currently sold commercially. The byproducts of the cross-coupling of organotrifluoroborates with organic halides are inorganic salts that are readily separable from the desired products. Finally, organotrifluoroborates can be employed in complex molecule synthesis in which a Suzuki−Miyaura cross-coupling to a valuable partner comprises a key transformation.[8]

Having previously established the efficiency and the advantages of the organotrifluoroborate partners in a variety of cross-coupling reactions,[6] we sought to extend their utility to systems not previously reported. Herein we report Suzuki−Miyaura cross-coupling reactions carried out between potassium aryl- and heteroaryltrifluoroborates and alkenyl bromides, which complements our previous efforts in the synthesis of unsaturated arenes using alkenyltrifluoroborates and aryl halides.[9]

Results and Discussion

Attention was initially focused on the determination of optimal conditions for the Suzuki−Miyaura cross-coupling reaction between potassium phenyltrifluoroborates (**1a**) and (*Z*)-(6-bromohex-5-enyloxy)-*tert*-butyldimethylsilane (**2a**), surveying the conditions in terms of catalysts, ligands, base, and solvents to obtain *tert*-butyldimethyl[(*Z*)-6-(phenyl)hex-5-enyloxy]silane (**3aa**, Table 1).

Initially, $Pd(OAc)_2$, PPh_3, and Cs_2CO_3 were employed in THF/H_2O at 70 °C overnight (19 h),[6c] obtaining 43% of the cross-coupled product **3aa** (Table 1, entry 1). Next, the catalyst was changed to a Pd(0) source, $Pd(PPh_3)_4$, resulting in a 51% yield of **3aa** in just 6 h (Table 1, entry 2). After settling on $Pd(PPh_3)_4$ as the catalyst, the solvent mixture was changed from THF/H_2O to toluene/H_2O (10:1) at 90 °C, thereby achieving a 92% yield of **3aa** (Table 1, entry 3). Even though fluoride is often used as a base in boronic acid mediated cross-coupling reactions, we and others have found that exogenous aqueous base is required for organotrifluoroborate cross-couplings.[6c,10] To re-establish this point, the reaction was performed under identical experimental conditions but in the absence of added base; only starting material was recovered after 7 h at 90 °C (Table 1, entry 4). Finally, efforts were made to increase the rate of the reaction while maintaining a high yield. By keeping the total toluene/H_2O solvent volume constant but decreasing the relative amount of toluene, the rate of the reaction was increased, and the reaction time could be decreased. Thus, employing 2 mol % of $Pd(PPh_3)_4$ in toluene/H_2O (2.6:1) at 90 °C provided a 97% yield of **3aa** in 35 min (Table 1, entry 5 or Table 2, entry 1). This procedure was utilized as the basis for all further studies. Under these conditions, the halide and catalyst were soluble in the organic phase, while the base dissolved in the water. Initially, the trifluoroborate was suspended in the reaction mixture. Over time, two homogeneous phases were created.

To test the generality of the method, potassium aryltrifluoroborates were chosen that possessed diverse functionalities (cyano, ether, aldehyde, halogen, and nitro groups, Table 2). For this aspect of the study, (*Z*)-(6-bromohex-5-enyloxy)-*tert*-

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(4) (a) Roques, B. P.; Florentin, D.; Callanquin, M. *J. Heterocycl. Chem.* **1975**, *12*, 195−196. (b) Roques, B. P.; Florentin, D.; Callanquin, M. *J. Heterocycl. Chem.* **1976**, *13*, 1265−1272. (c) Kuivila, H. G.; Nahabedian K. V. *J. Am. Chem. Soc.* **1961**, *83*, 2159−2163.

(5) Wong, M. S.; Zhang, X. L. *Tetrahedron Lett.* **2001**, *42*, 4087−4089.

(6) (a) Molander, G. A.; Biolatto, B. *Org. Lett.* **2001**, *3*, 393−396. (b) Molander, G. A.; Biolatto, B. *Org. Lett.* **2002**, *4*, 1867−1870. (c) Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302−4314. (d) Molander, G. A.; Katona, B. W.; Machrouhi, F. *J. Org. Chem.* **2002**, *67*, 8416−8423. (e) Molander, G. A.; Yun, C. S.; Ribagorda, M.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 5534−5539. (f) Molander, G. A.; Ribagorda, M. *J. Am. Chem. Soc.* **2003**, *125*, 11148−11149. (g) Molander, G. A.; Felix, L. A. *J. Org. Chem.* **2005**, *70*, 3950−3956. (h) Molander, G. A.; Figueroa, R. *Aldrichimica Acta* **2005**, *38*, 49−55.

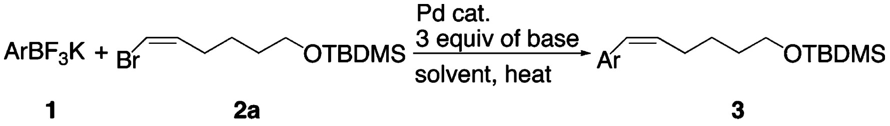
(7) (a) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020−3027. (b) Vedejs, E.; Fields, S. C.; Hayashi, R.; Hitchcock, S. R.; Powell, D. R.; Schrimpf, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 2460−2470.

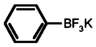
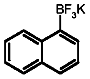
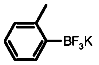
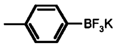
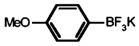
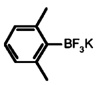
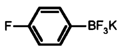
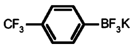
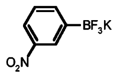
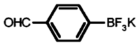
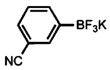
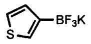
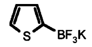
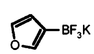
(8) (a) Molander, G. A.; Dehmel, F. *J. Am. Chem. Soc.* **2004**, *126*, 10313−10318. (b) Skaff, O.; Jolliffe, K. A.; Hutton, C. A. *J. Org. Chem.* **2005**, *70*, 7353−7363. (c) García-Fortanet, J.; Debergh, J. R.; De Brabander, J. K. *Org. Lett.* **2005**, *7*, 685−688. (d) Toyota, M.; Asano, T.; Ihara, M. *Org. Lett.* **2005**, *7*, 3929−3932.

(9) Molander, G. A.; Bernardi, C. *J. Org. Chem.* **2002**, *67*, 8424−8429.

(10) (a) Batey, R. A.; Quach, T. D. *Tetrahedron Lett.* **2001**, *42*, 9099−9103. (b) Yuen, A. K. L.; Hutton, C. A. *Tetrahedron Lett.* **2005**, *46*, 7899−7903.

TABLE 2. Cross-Coupling Reaction of Potassium Aryltrifluoroborates with (*Z*)-(6-Bromohex-5-enyloxy)-*tert*-butyldimethylsilane



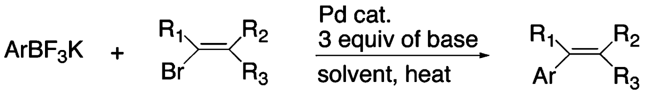
entry	ArBF$_3$K	reaction conditions [a]	% isolated yield
1	 **1a**	A, 35 min	**3aa**, 97
2	 **1b**	A, 50 min	**3ba**, >99
3	 **1c**	A, 1.5 h	**3ca**, 91
4	 **1d**	A, 25 min	**3da**, 93
5	 **1e**	A, 40 min[b]	**3ea**, 97
6	 **1f**	A, 2.8 h [b,c]	**3fa**, 82
7	 **1g**	A, 55 min[b]	**3ga**, 95
8	 **1h**	A, 3 h [b,c,d]	**3ha**, 89
9	 **1i**	A, 2.5 h [b,f]	**3ia**, 90 (>87[i])
10	 **1j**	A, 3.5 h [b,f]	**3ja**, 89
11	 **1k**	A, 7.5 h [b,e,f]	**3ka**, 86
12	 **1l**	A, 2.5 h [b,c,g]	**3la**, >99
13		A, 3.5 h [b,h]	**3la**, 93
14	 **1m**	A, 2.5 h [b,c,g]	**3ma**, 80
15	 **1n**	A, 2.5 h [b,c,g]	**3na**, 98

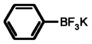
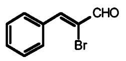
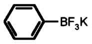
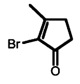
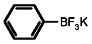
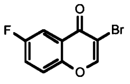
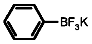
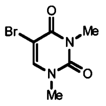
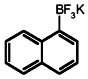
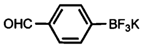
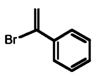
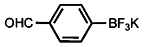
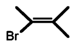
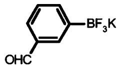
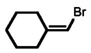
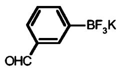
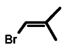
[a] Condition A: 2 mol % of Pd(PPh$_3$)$_4$, toluene:H$_2$O (2.6:1), 3 equiv of Cs$_2$CO$_3$, 90 °C, under N$_2$. [b] The reaction was carried out with K$_2$CO$_3$ instead of Cs$_2$CO$_3$. [c] The reaction was carried out with 4.5 mol % of Pd(PPh$_3$)$_4$. [d] The reaction was carried out with 9 mol % of P(Bu)$_3$. [e] The reaction was carried out at 55 °C. [f] The reaction was carried out with 4.5 mol % of Pd(dppf)•CH$_2$Cl$_2$. [g] The reaction was not optimized for time or mol % of catalyst loaded. [h] The reaction was carried out with 0.5 mol % of Pd(PPh$_3$)$_4$. [i] GC purity.

butyldimethylsilane (**2a**) was again selected as the standard electrophile. The reactions conducted led to very high yields of the cross-coupled product, with reaction times varying between 25 min and 3.5 h (with the exception of entry 11, Table 2). The reaction results confirm the stereospecificity of the reaction and the compatibility of silyl ether protecting groups with the reaction conditions. The latter point was previously a concern because the trifluoroborates represent an obvious source of fluoride that is often used to deprotect silylated alcohols. The protecting group stability is perhaps due to the heterogeneous nature of the system in which the fluoride is solvated in the aqueous layer and thus unavailable to deprotect the organic soluble silyl ether.[6g]

Electron-neutral potassium aryltrifluoroborates were examined, starting with potassium 1-naphthyltrifluoroborate **1b**. The reaction was complete in 50 min, affording a quantitative yield of **3ba** (Table 2, entry 2). To begin an evaluation of steric and electronic effects, potassium 4-tolyl- (**1d**), potassium 2-tolyl- (**1c**), and potassium 2,6-dimethylphenyltrifluoroborate **1f** were examined in which inductively electron-donating substituents were present. Potassium 4-tolyl-trifluoroborate was the fastest, with the product **3da** being obtained in 93% yield in 25 min

TABLE 3. Cross-Coupling Reaction of Potassium Aryltrifluoroborates with Bromoalkenes



entry	$ArBF_3K$	alkene	reaction conditions [a]	% isolated yield
1	 **1a**	 **2c**	A, 30 min	**3ac**, 94
2	 **1a**	 **2d**	A, 1.8 h	**3ad**, 87
3	 **1a**	 **2e**	A, 1 h	**3ae**, 87
4	 **1a**	 **2f**	A, 3 h	**3af**, 88
5	 **1b**	 **2b**	A, 1 h	**3bb**, 94
6	 **1j**	 **2g**	A, 3 h [b]	**3jg**, 89
7	 **1j**	 **2h**	A, 2 h [b]	**3jh**, 94
8	 **1o**	 **2i**	A, 1 h [b]	**3oi**, 85
9	 **1o**	 **2j**	A, 1.5 h [b]	**3oj**, 96

[a] Condition A: 2 mol % of $Pd(PPh_3)_4$, toluene:H_2O (2.6:1), 3 equiv of K_2CO_3, 90 °C, under N_2. [b] The reaction was carried out with 2 mol % of $Pd(dppf)\cdot CH_2Cl_2$ instead of $Pd(PPh_3)_4$.

(Table 2, entry 4). Potassium 2-tolyl-trifluoroborate is more sterically hindered, and the synthesis of **3ca** was realized in 91% yield after 1.5 h (Table 2, entry 3). Potassium 2,6-dimethylphenyltrifluoroborate, the most sterically hindered of the trio, required 4.5 mol % of catalyst to achieve an 82% yield of **3fa** in 2.8 h (Table 2, entry 6). An identical reaction charged with 2 mol % of catalyst resulted in about 64% yield of the desired product after 5 h as determined by ^1H NMR spectroscopy. As the steric hindrance of the substrates increased, protodeborination became more important, leaving some of the bromoalkene unreacted.

To decrease the reaction cost, all of the remaining reactions (including **3fa**, Table 2, entry 6) were performed with K_2CO_3 instead of Cs_2CO_3. Thus, potassium 4-methoxyphenyltrifluoroborate **1e** and potassium 4-fluorophenyltrifluoroborate **1g** were tested, as these substituents have π-releasing but inductively electron-withdrawing characteristics. The reaction with **1e** was complete in 40 min, providing a 97% yield of **3ea** (Table 2, entry 5). In a similar manner, product **3ga** was obtained in 95% yield from substrate **1g** after 55 min (Table 2, entry 7).

To access the product (**3ha**, 89% yield, 3 h) from the coupling between the electron-deficient aryltrifluoroborate **1h** and alkenyl halide **2a**, it was necessary to employ 9 mol % of $(Bu)_3P$ as the phosphine ligand (Table 2, entry 8). For the remaining electron-poor aryltrifluoroborates, 4.5 mol % of the less expensive and more stable $PdCl_2(dppf)\cdot CH_2Cl_2$ was employed, which performed better than 4.5 mol % of Pd(PPh_3)$_4$ (Table 2, entry 8). In this manner, potassium 4-nitrophenyltrifluoroborate **1i** provided the cross-coupled product **3ia** in 90% yield (Table 2, entry 9), which was ≥87% pure by capillary GC analysis. Unfortunately in this case, it was not possible to remove an unknown byproduct by silica gel column chromatography. Other electron-deficient arylborons worked equally well under these conditions. Thus, potassium 4-trifluoroboratobenzaldehyde **1j** yielded the product **3ja** in 89% yield (Table 2, entry 10), and potassium 3-cyanophenyltrifluoroborate **1k** gave the product **3ka** in 86% yield (Table 2, entry 11).

Potassium heteroaryltrifluoroborates were examined using the same catalyst [Pd(PPh_3)$_4$] as that employed for electron-rich aryltrifluoroborates (**1l**, **1m**, and **1n**). Thus, 3-trifluoroboratothiophene **1l** was cross-coupled with **2a**, and after 2.5 h, **3la** was generated in quantitative yield (Table 2, entry 12). To demonstrate that the method is suitable for large-scale reactions, where the amount of catalyst is a concern, the same reaction was performed with a lower catalyst loading [0.5 mol % of Pd(PPh_3)$_4$]. Under these conditions, the reaction took longer (3.5 h as opposed to 2.5 h with 2 mol % of catalyst), but still gave a 93% yield of product **3la** (Table 2, entry 13). Cross-coupling of potassium 2-trifluoroboratothiophene **1m** and alkenyl bromide **2a** yielded **3ma** in 80% yield (Table 2, entry 14). Potassium 3-trifluoroboratofuran afforded 98% of the cross-coupled product in 2.5 h (Table 2, entry 15).

Continuing with the investigation, the scope of the reaction with regard to the bromoalkenes was examined. Haloalkenes containing a variety of functional groups (α,β-unsaturated ketones, α,β-unsaturated aldehydes, α,β-unsaturated amides), as well as substitution patterns (trisubstituted bromoalkenes, tetrasubstituted bromoalkenes, and ω-halogenobromoalkenes), all proved to be successful coupling partners (Table 3).

The products resulting from coupling of **1a** with (*E*)-2,3-diphenylpropenal, 3-methyl-2-phenyl-2-cyclopent-2-enone, 6-fluoro-3-phenylchromen-4-one, and 1,3-dimethyl-5-phenyl-1*H*-pyrimidine-2,4-dione (**3ac**, **3ad**, **3ae**, **3af**, respectively) were all obtained as white solids. α-Bromocinnamaldehyde **2c** was coupled with **1a**, leading to the desired product **3ac** in 94% yield in 30 min (Table 3, entry 1). The reaction of 2-bromo-3-methyl-2-cyclopenten-1-one **2d** afforded the product **3ad** in 87% yield after a longer period of time (1.8 h, Table 3, entry 2). Products **3ae** and **3af** were recrystallized and obtained in 87 (1 h) and 88% yield (3 h), respectively (Table 3, entries 3 and 4). The cross-coupling reaction between (*Z*)-1-bromo-6-chlorohex-1-ene **2b** and potassium 1-naphthalenetrifluoroborate **1b** yielded, without further purification, 94% of product **3bb** in 1 h (Table 3, entry 5). The reaction with α-bromostyrene **2g** was carried out with **1a**, using 2 mol % of Pd(PPh_3)$_4$ to give a crude product that was difficult to separate from the biphenyl byproduct. However, utilizing 4-trifluoroboratobenzaldehyde **1j** in conjunction with **2g** and 2 mol % of $PdCl_2$(dppf)•CH_2Cl_2 as the catalyst allowed access to the corresponding product in 89% yield in 3 h. This product, **3jg**, possessed higher polarity and silica gel affinity than the biphenyl from **1a**, and so it proved possible to separate it cleanly from the minor homocoupling byproduct formed. Finally, trisubstituted and tetrasubstituted bromoalkenes (**2h**, **2i**, **2j**) were explored. The product from the tetrasubstituted bromoalkene, **3jh**, required a longer reaction time compared to that of **3oi** and **3oj** (Table 3, entries 7−9), but yields for all three were excellent.

Conclusions

In summary, the palladium-catalyzed cross-coupling reactions of potassium aryl- and heteroaryltrifluoroborates with alkenyl halides were achieved in good to excellent yields. The procedure possesses several advantages when compared with other methods. The potassium aryltrifluoroborates can be prepared easily by different routes, and the ease of isolation, purification, handling, and long-term storage makes them attractive intermediates for large scale use as well. The cross-coupling can be carried out rapidly using as little as 0.5 mol % of catalyst loading along with an inexpensive inorganic base. For electron-neutral and electron-rich aryltrifluoroborates, Pd(PPh_3)$_4$ is suitable for the cross-coupling, while $PdCl_2$(dppf)•CH_2Cl_2 has proven to be more efficient in the coupling of electron-deficient aryltrifluoroborates.

When (*Z*)-bromoalkenes are employed, the (*Z*)-styryl moiety is achieved stereospecifically, and silyl protecting groups for alcohols are tolerated even though a fluoride source is present. Moreover, a variety of other functional groups (aldehydes, ketones, enones, nitriles, and nitro groups) and substitution patterns are tolerated in both coupling partners.

Experimental Section

General Procedure for Suzuki−Miyaura Cross-Coupling Reactions. Preparation of *tert*-Butyldimethyl[(*Z*)-6-(phenyl)hex-5-enyloxy]silane (3aa). In a 13 × 100 mm test tube were weighed Cs_2CO_3 (1.13 mmol, 366.0 mg), **1a** (0.42 mmol, 80.0 mg), Pd(PPh_3)$_4$ (0.0074 mmol, 8.6 mg, 2 mol %), and **2a** (0.38 mmol, 116.2 mg). A septa was placed on the test tube which then was purged with N_2 for 2 min. The solvents (1 mL of toluene and 0.375 mL of H_2O) were added, and the test tube was put in an oil bath previously set at 90 °C. The reaction was monitored by TLC with hexanes as eluent. After 35 min, when the reaction was complete, it was diluted with hexanes, and $MgSO_4$ was added. The organic layer was removed, and the remaining $MgSO_4$ paste was triturated five times with hexanes. The combined organic extracts were added directly to a plug of silica gel to remove the catalyst, thus yielding the crude product. Further purification was accomplished via column chromatography (SiO_2, hexanes), yielding a colorless oil (107.1 mg, 97%).

IR (neat): ν 3009.4, 1600.2, 1494.1, 1471.8, 1462.31, 1255.4, 1104.3 cm^{-1}. ^{1}H NMR ($CDCl_3$, 360 MHz): δ 7.30 (m, 5H), 6.46 (d, $J = 11.7$ Hz, 1H), 5.70 (dt, $J = 11.7$, 7.3 Hz, 1H), 3.64 (t, $J = 6.1$ Hz, 2H), 2.39 (m, 2H), 1.56 (m, 4H), 0.93 (s, 9H), 0.08 (s, 6H). ^{13}C NMR ($CDCl_3$, 90 MHz): δ 137.7, 132.9, 128.9, 128.7, 128.1, 126.4, 62.9, 32.5, 28.3, 26.2, 25.9, 18.3, −5.3. HRMS (CI): *m*/*z* calcd for $C_{18}H_{31}OSi$ (MH^+) 291.2144, found 291.2141.

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Supporting Information Available: Experimental details and structural data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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