JOC Article

Scope of the Suzuki−Miyaura Cross-Coupling Reaction of Potassium Trifluoroboratoketohomoenolates

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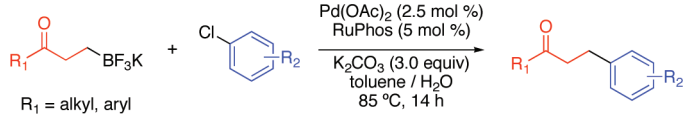
Received November 3, 2008

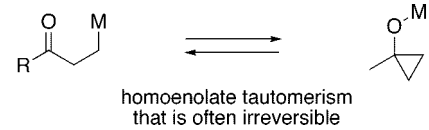


Potassium trifluoroboratoketohomoenolates were prepared in good yields from either the corresponding α,β-unsaturated compounds or methyl ketones. These organoboron reagents were effectively cross-coupled with various aryl and heteroaryl chlorides.

Introduction

Reactions in which the normal charge affinity patterns are reversed are of great interest in organic synthesis because unique means of forming carbon−carbon bonds can be envisioned. The homoenolate is an archetypal synthon within this paradigm of umpolung reactivity:[1] it is a nucleophile and thus serves as an inverse-polarity synthon of a Michael acceptor.

Homoenolates have proven to be highly effective reagents in acylations,[2] nucleophilic additions such as aldol-type reactions,[3] and metal-catalyzed cross-coupling reactions,[4] but the main challenge in using these reagents comes from their preparation. Even though homoenolates can be prepared by deprotonation of carbonyl compounds,[5] generally the low acidity of the protons in the β-position in combination with the instability of the resulting homoenolates makes this approach prohibitive. Alternatively, metallohomoenolates can be reliably prepared via a ring opening of siloxycyclopropanes using Lewis acidic metals such as titanium[3c,6] and zinc.[2a,4a,7] A further difficulty associated with homoenolates is the spontaneous cyclization to the cyclopropanoxide isomer that prevents nucleophilic reaction toward electrophiles (eq 1).[8] This issue is more pronounced with highly electrophilic carbonyl groups[5b] and explains why β-metallo esters have been used extensively for carbon−carbon bond-forming reactions, in stark contrast to the near-absence of β-metallo ketones.[9]



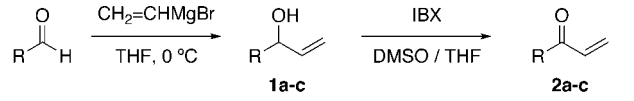
(1)

In terms of cross-coupling reactions, zinc ketohomoenolates have been prepared and used in palladium-catalyzed reaction with acid chlorides,[9a] but to the best of our knowledge neither these nor tin[10] or boro[11] ketohomoenolates have been employed in metal-catalyzed cross-coupling reactions with aryl electrophiles. Therefore, the ability to form homoenolates of ketones that can react to form carbon−carbon bonds is of significant interest.

(1) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.
(2) (a) Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1984**, *106*, 3368. (b) Tamaru, Y.; Ochiai, H.; Nakamura, T.; Tsubaki, K.; Yoshida, Z. *Tetrahedron Lett.* **1985**, *26*, 5559. (c) Nakamura, E.; Aoki, S.; Sekiya, K.; Oshino, H.; Kuwajima, I. *J. Am. Chem. Soc.* **1987**, *109*, 8056.
(3) (a) Goswami, R. *J. Org. Chem.* **1985**, *50*, 5907. (b) Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1983**, *105*, 652. (c) Martins, E.; Gleason, J. *Org. Lett.* **1999**, *1*, 1643. (d) Ochiai, H.; Nishihara, T.; Tamaru, Y.; Yoshida, Z. *J. Org. Chem.* **1988**, *53*, 1343. (e) McWilliams, J. C.; Armstrong, J. D., III; Zheng, N.; Bhupathy, M.; Volante, R. P.; Reider, P. J. *J. Am. Chem. Soc.* **1996**, *118*, 11970.
(4) (a) Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 83. (b) Rilatt, I.; Caggiano, L.; Jackson, R. F. W. *Synlett* **2005**, *18*, 2701. (c) Scherer, S.; Meudt, A.; Nerdinger, S.; Lehnemann, B.; Jagusch, T.; Snieckus, V. Patent WO 2006/097221, 2006.
(5) (a) Nickon, A.; Lambert, J. L. *J. Am. Chem. Soc.* **1962**, *84*, 4004. (b) Shiner, C. S.; Berks, A. H.; Fisher, A. M. *J. Am. Chem. Soc.* **1988**, *110*, 957.
(6) Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1977**, *99*, 7360.
(7) (a) Oshimo, H.; Nakamura, E.; Kuwajima, I. *J. Org. Chem.* **1985**, *50*, 2804. (b) Nakamura, E.; Sekiya, K.; Kuwajima, I. *Tetrahedron Lett.* **1987**, *28*, 337.
(8) Kuwajima, I.; Nakamura, E. In *Comprehensive Organic Synthesis*; Trost, B., Fleming, I., Eds; Pergamon: Oxford, 1991: Vol. 2, p 441.
(9) (a) Tamaru, Y.; Ochia, H.; Nakamura, T.; Yoshida, Z. *Angew. Chem., Int. Ed.* **1987**, *26*, 1157. (b) Aoki, S.; Fujimura, T.; Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1988**, *110*, 3296. (c) Fujimara, T.; Aoki, S.; Nakamura, E. *J. Org. Chem.* **1991**, *56*, 2809.
(10) (a) Burley, J. W.; Hutton, R.; Oakes, V. *J. Chem. Soc., Chem. Commun.* **1976**, 803. (b) Nakashira, H.; Ryu, I.; Ogawa, A.; Kambe, N.; Sonoda, N. *Organometallics* **1990**, *9*, 277. (c) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4336. (d) Nakamura, E.; Shimada, J.; Kuwajima, I. *Organometallics* **1985**, *4*, 641.

10.1021/jo802453m CCC: $40.75 © 2009 American Chemical Society
Published on Web 01/09/2009

SCHEME 1



The value of organoboron cross-coupling reagents has been widely described in the literature. In addition to their functional group tolerance, they also exhibit low toxicity. Boron homoenolates can be prepared either by alkylation of a halomethyl boronate[11a,12] or by 1,4-addition of bis(pinacolato)diboron to α,β-unsaturated carbonyl derivatives.[11b,c,13] Surprisingly, outside of our first report,[14] only a single example using boron homoenolates in Suzuki−Miyaura cross-coupling reaction has been reported in the literature, and this involved the transformation of ester homoenolates.[4c]

Potassium organotrifluoroborates represent a novel class of organoborons that possess physical and chemical properties that make them attractive alternatives to the classic boronic acids and boronate esters for use in organic synthesis. The organotrifluoroborates are crystalline compounds that are indefinitely stable to moisture and air.[15] Their monomeric form, coupled with their lower tendency to protodeboronate as compared to boronic acids,[16] permits the use of stoichiometric amounts of these nucleophiles for cross-coupling reactions.[17] We recently reported an efficient synthesis of various potassium trifluoroboratohomoenolates and showed that they are effective coupling partners in the Suzuki−Miyaura reaction.[14] To the best of our knowledge, this was the first example of the cross-coupling of ketone- and amide-containing homoenolates.

To expand the scope of this method, we prepared a larger variety of ketone homoenolates derived from both aromatic and aliphatic ketones. Herein, we report the preparation of several potassium trifluoroboratoketohomoenolates and their coupling with a wide variety of aryl and heteroaryl chlorides.

Results and Discussion

Initially, we prepared an array of potassium trifluoroboratoketohomoenolates using two different procedures. First, aliphatic trifluoroboratoketohomoenolates were generated via the conjugate addition of bis(pinacolato)diboron to unsaturated ketones as reported by Yun and co-workers.[13a] The starting α,β-unsaturated ketones were prepared via the following sequence: commercially available aldehydes were treated with vinylmagnesium bromide, and the resulting allylic alcohols **1a**−**c** were then oxidized using IBX to give ketones **2a**−**c** in good to excellent yields[18,19] (Scheme 1).

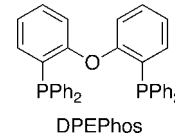
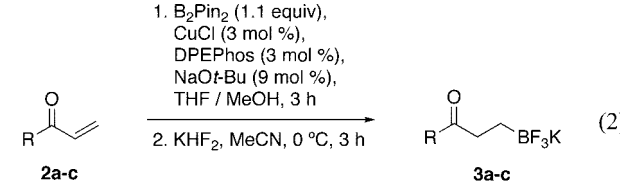


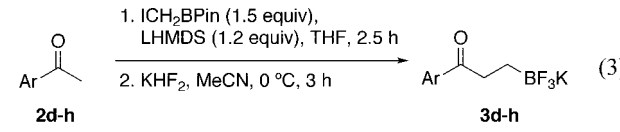
FIGURE 1. DPEPhos ligand.

With these α,β-unsaturated ketones in hand, organoboron reagents were then prepared according to the conditions of Yun and co-workers[13a] by using a combination of CuCl, DPEPhos (Figure 1), and NaO*t*-Bu. The resulting pinacolboronates were subsequently converted to the corresponding potassium organotrifluoroborates by quenching with KHF_2 (Strategy A, eq 2, Table 1). The aliphatic trifluoroboratoketohomoenolates were obtained in good yields.



Strategy A

Unfortunately, we could not prepare the aryl ketone derivatives using this procedure, and an alternative route was investigated. Using commercially available aromatic ketones, a deprotonation by LHMDS followed by the addition of iodomethylpinacolboronate[12c] and quenching with KHF_2 led to the desired aromatic trifluoroboratoketohomoenolates in good yields (Strategy B, eq 3, Table 1). Purification of the different trifluoroboratohomoenolates prepared by either method was accomplished using either Soxhlet extraction or filtration/hot filtration in acetone,[20] depending on their solubilities.



Strategy B

With the requisite trifluoroboratohomoenolates in hand, Suzuki cross-coupling reactions were next examined. A preliminary study had shown that a trifluoroboratoketohomoenolate cross-coupled in good yields with aryl bromides and selected aryl chlorides.[14] These results prompted us to expand the study, using the more stable and less expensive aryl chlorides as the coupling partner to examine the scope of this method. On the basis of the optimized conditions previously reported,[14] we initially conducted the cross-coupling of trifluoroboratohomoenolate **3a** with electron-poor aryl chlorides (Table 2) in the presence of $Pd(OAc)_2$ (2.5 mol %) and RuPhos (Figure 2, 5 mol %) using K_2CO_3 as a base and a mixture of toluene/H_2O as the solvent system. All of the electrophiles gave rise to the

(11) (a) Mears, R. J.; Sailes, H. E.; Watts, J. P.; Whiting, A. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3250. (b) Lawson, Y. G.; Lesley, M. J. G.; Marder, T. B.; Norman, N. C.; Rice, C. R. *Chem. Commun.* **1997**, 2051. (c) Takahashi, K.; Ishiyama, T.; Miyaura, N. *Chem. Lett.* **2000**, 982. (d) Ito, H.; Yamanaka, H.; Tateiwa, J.; Hosomi, A. *Tetrahedron Lett.* **2000**, *41*, 6821. (e) Kabalka, G. W.; Das, B. C.; Das, S. *Tetrahedron Lett.* **2002**, *43*, 2323.

(12) (a) Matteson, D. S.; Cheng, T.-C. *J. Org. Chem.* **1968**, *33*, 3055. (b) Matteson, D. S.; Beedle, D. S. *Tetrahedron Lett.* **1987**, 4499. (c) Whiting, A. *Tetrahedron Lett.* **1991**, *32*, 1503.

(13) (a) Mun, S.; Lee, J.-E.; Yun, J. *Org. Lett.* **2006**, *8*, 4887. (b) Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2007**, *9*, 5031.

(14) Molander, G. A.; Petrillo, D. E. *Org. Lett.* **2008**, *10*, 1795.

(15) For reviews of organotrifluoroborate salts, see: (a) Darses, S.; Genêt, J.-P. *Chem. Rev.* **2008**, *108*, 288. (b) Molander, G. A.; Figueroa, R. *Aldrichimica Acta* **2005**, *38*, 49. (c) Darses, S.; Genêt, J.-P. *Eur. J. Org. Chem.* **2003**, 4313. (d) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275. (e) Stefani, H. A.; Cella, R.; Vieira, A. S. *Tetrahedron* **2007**, *63*, 3623.

(16) Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302.

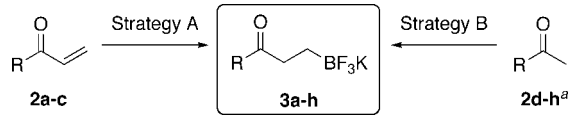
(17) Molander, G. A.; Jean-Gérard, L. *J. Org. Chem.* **2007**, *72*, 8422. (b) Molander, G. A.; Gormisky, P. E.; Sandrock, D. L. *J. Org. Chem.* **2008**, *73*, 2052. (c) Molander, G. A.; Canturk, B. *Org. Lett.* **2008**, *10*, 2135.

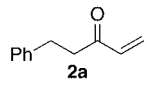
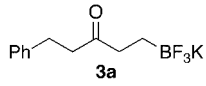
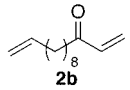
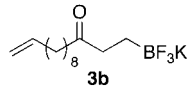
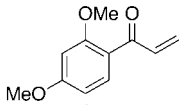
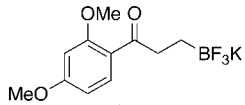
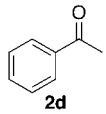
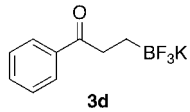
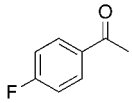
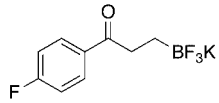
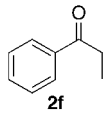
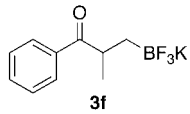
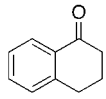
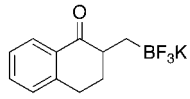
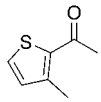
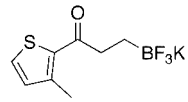
(18) Depending on the commercial source, vinylmagnesium bromide permitted the formation of the α,β-unsaturated ketones in quantitative yield over the two steps.

(19) Nicolaou, K. C.; Lim, Y. H.; Piper, J. L.; Papageorgiou, C. D. *J. Am. Chem. Soc.* **2007**, *129*, 4001.

(20) See Supporting Information for details of all of the purification procedures.

TABLE 1. Preparation of Potassium Trifluoroboratoketohomoenolates 3a−h

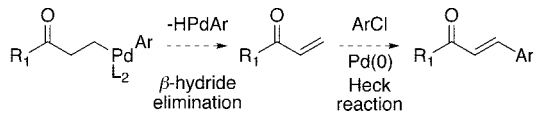


entry	reactant	RBF_3K	% isolated yield
1	 **2a**	 **3a**	60[b]
2	 **2b**	 **3b**	41[b]
3	 **2c**	 **3c**	57[b]
4	 **2d**	 **3d**	63[c]
5	 **2e**	 **3e**	70[c]
6	 **2f**	 **3f**	73[c]
7	 **2g**	 **3g**	75[c]
8	 **2h**	 **3h**	73[c]

[a] Starting methyl ketones were freshly distilled from commercial sources. [b] Strategy A: B_2Pin_2 (1.5 equiv), 3% CuCl, 3% DPEPhos, 9% NaO*t*-Bu, THF/MeOH, 3 h, then KHF_2 (aq); overall yield. [c] Strategy B: ICH_2BPin (1.5 equiv), LHMDS (1.2 equiv), THF, 2.5 h, then KHF_2 (aq); overall yield.

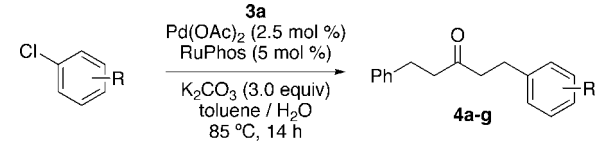
corresponding products in good to excellent yields. Many functional groups were tolerated in the ortho, meta, or para position including an aldehyde, a ketone, an ester, and a nitrile. It is noteworthy that these reactions were efficient even using only a slight excess (1%) of the organotrifluoroborate.

Importantly, there was little to no formation of the Heck product resulting from the β-hydride elimination of the palladium(II) homoenolate intermediate and subsequent addition of an organopalladium species derived from the aryl chloride (eq 4).



(4)

TABLE 2. Cross-Coupling of the Potassium Organotrifluoroborate 3a with Various Electron-Poor Aryl Chlorides



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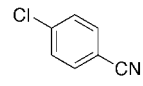
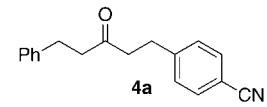
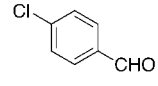
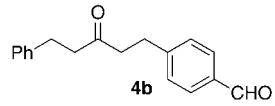
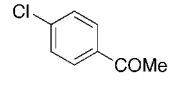
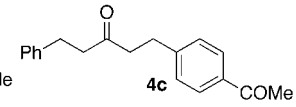
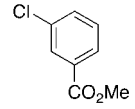
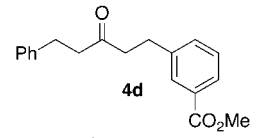
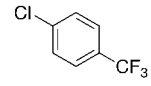
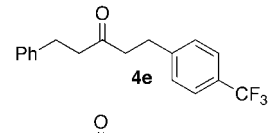
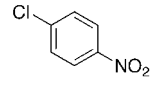
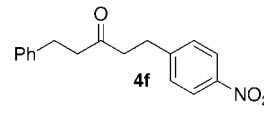
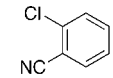
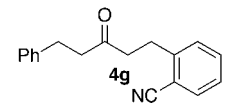
1		 **4a**	73
2		 **4b**	94
3		 **4c**	80
4		 **4d**	89
5		 **4e**	82
6		 **4f**	75
7		 **4g**	81

[a] All reactions were carried out using 0.25 mmol of aryl chloride and 0.2525 mmol of potassium organotrifluoroborate **3a**.

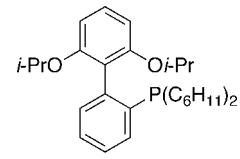
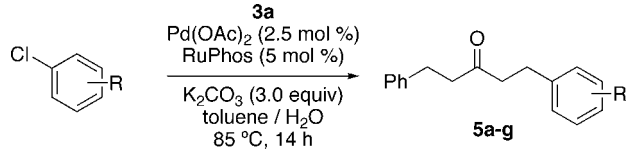


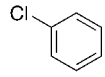
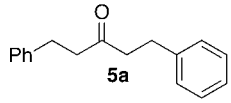
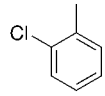
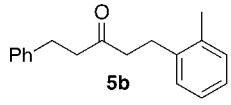
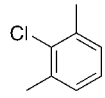
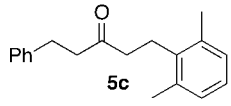
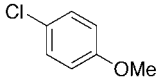
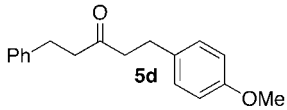
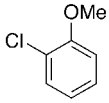
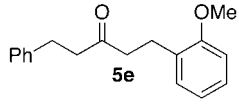
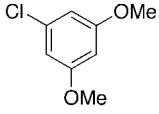
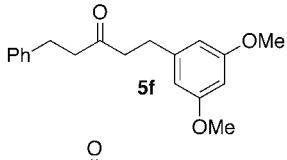
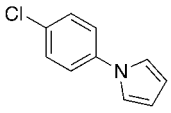
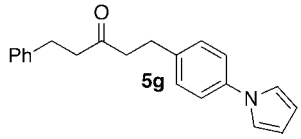
FIGURE 2. RuPhos ligand.

The scope of this method was then expanded using the potassium trifluoroboratohomoenolate **3a** in conjunction with various electron-rich aryl chlorides (Table 3). The desired cross-coupled products were obtained in good yields even though the electron-rich aryl chlorides are known to be more difficult coupling partners than the electron-deficient chlorides.[21] The use of sterically hindered electrophiles such as 2-chloro-1,3-dimethylbenzene (entry 3) did not affect the efficiency of the reaction. In addition, ortho-, meta-, and para-substituted deriva-

(21) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed. Engl.* **2002**, *41*, 4176.

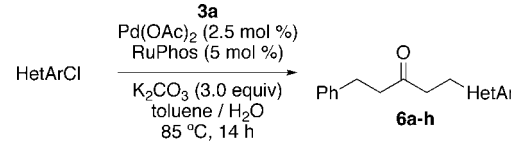
TABLE 3. Cross-Coupling of the Potassium Organotrifluoroborate 3a with Various Electron-Rich Aryl Chlorides

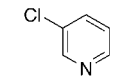
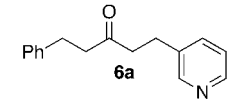
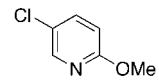
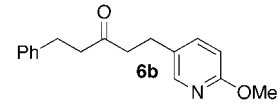
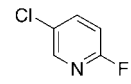
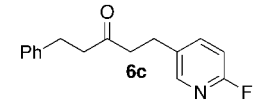
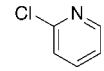
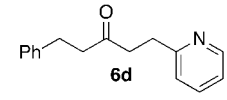
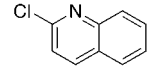
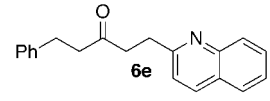
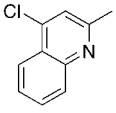
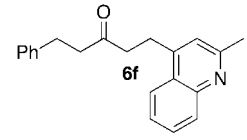
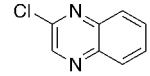
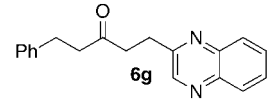
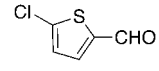
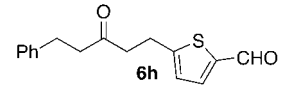


entry	aryl chloride	product	% isolated yield
1		 **5a**	83
2		 **5b**	70
3		 **5c**	67
4		 **5d**	78
5		 **5e**	88
6		 **5f**	89(90)[b]
7		 **5g**	89

[a] All reactions were carried out using 0.25 mmol of aryl chloride and 0.2525 mmol of potassium organotrifluoroborate **3a**. [b] This reaction was performed on a 2.0 mmol scale.

TABLE 4. Cross-Coupling of Potassium Organotrifluoroborate 3a with Heteroaryl Chlorides



entry	heteroaryl chloride	product	% isolated yield
1		 **6a**	72
2		 **6b**	87
3		 **6c**	73
4		 **6d**	/
5		 **6e**	60
6		 **6f**	65
7		 **6g**	43
8		 **6h**	60

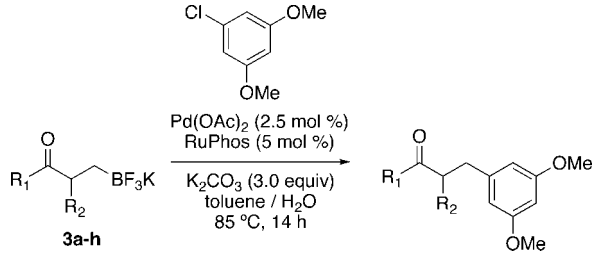
[a] All reactions were carried out using 0.25 mmol of aryl chloride and 0.2525 mmol of potassium organotrifluoroborate **3a**.

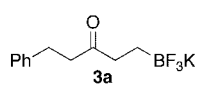
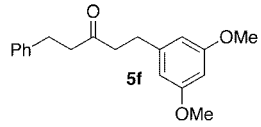
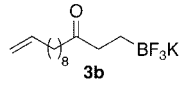
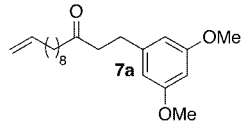
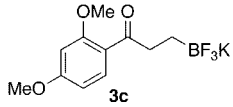
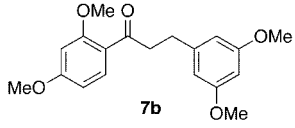
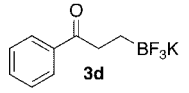
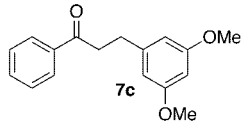
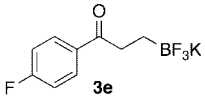
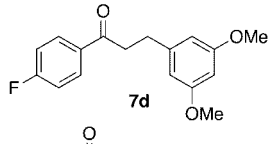
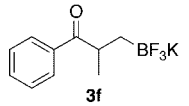
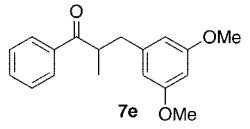
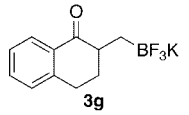
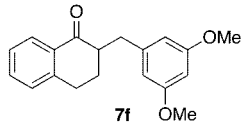
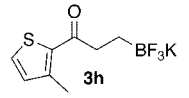
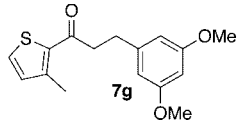
tives were all effective substrates for the coupling. The reaction could also be scaled efficiently to 2.0 mmol of aryl chloride (entry 6).

To investigate the method further, we expanded the array of electrophiles to heteroaromatic chlorides (Table 4). Most of the heteroaryl chlorides cross-coupled and provided the coupled products in good yields. Unfortunately, 2-chloropyridine (entry 4) was not a successful coupling partner under these conditions, but surprisingly, 2-chloroquinoline (entry 5) gave rise to the desired coupled derivative in synthetically useful yield. Interestingly, 2-chloroquinoxaline gave the expected cross-coupled product, but in moderate yield (entry 7).

To demonstrate the scope of the method further, different trifluoroboratohomoenolates were cross-coupled with 5-chloro-1,3-dimethoxybenzene (Table 5). The aliphatic derivatives **3a** and **3b** cross-coupled with this electrophile, but we obtained only trace amounts of the expected product from most of the studied aromatic trifluoroborates (Table 5, entries 4, 5, 7, and 8). Surprisingly, the α-substituted aromatic trifluoroborate **3f** provided the expected product in contrast to the tetralone derivative **3g**. Optimization of the reaction conditions was attempted using the thiophene derivative (Table 5, entry 8), but the results were not satisfactory. Therefore, we studied the electrophiles that could be used with these aromatic substrates, and we initially utilized electron-rich aryl chlorides to determine whether the 5-chloro-1,3-dimethoxybenzene was simply a problematic electrophile (Table 6, entries 1 and 2). The coupling of these aromatic ketone-containing trifluoroborates proved to be challenging with all electron-rich aryl chlorides studied, but when 1-bromo-3,5-dimethoxybenzene (the bromide analog of the electrophile used in Table 5) and 3-bromoanisole were used, good yields of the coupled product were obtained (Table 6, entries 3 and 4). Electron-deficient electrophiles were then utilized, and both the chloride and the bromide derivatives provided the desired product (Table 6, entries 5 and 6).

TABLE 5. Cross-Coupling of Various Potassium Trifluoroboratohomoenolates with 5-Chloro-1,3-Dimethoxybenzene

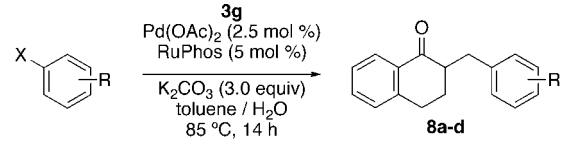


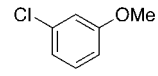
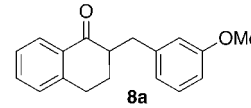
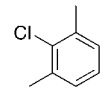
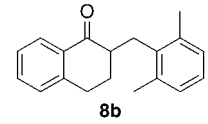
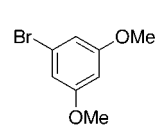
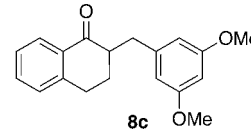
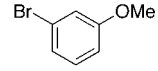
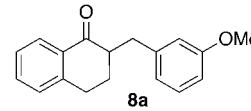
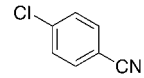
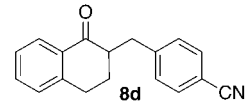
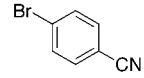
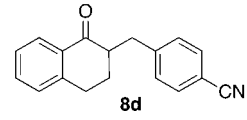
entry	RBF_3K	product	% isolated yield
1	 **3a**	 **5f**	89
2	 **3b**	 **7a**	81
3	 **3c**	 **7b**	87
4	 **3d**	 **7c**	trace
5	 **3e**	 **7d**	trace
6	 **3f**	 **7e**	60
7	 **3g**	 **7f**	trace
8	 **3h**	 **7g**	trace(35[b])

[a] All reactions were carried out using 0.25 mmol of the aryl chloride and 0.2525 mmol of potassium organotrifluoroborates. [b] $Pd(OAc)_2$ (5 mol %) and RuPhos (10 mol %) were used.

With these results in hand, we next cross-coupled aromatic trifluoroboratoketohomoenolates with 3-bromoanisole as the electrophile (Table 7). All of the ketohomoenolates coupled in yields better than those observed with the electron-rich aryl chloride (Table 5), including the heteroaryl trifluoroborate **3h** (Table 7, entry 6). These results indicate a surprising difference of reactivity between the aliphatic ketone-containing trifluoroboratohomoenolate and the aromatic derivatives toward diverse aromatic electrophiles, a result whose genesis is not easily understood.

TABLE 6. Effect of the Nature of the Electrophile on the Cross-Coupling with the Aromatic Ketone-Containing Trifluoroboratohomoenolate 3g



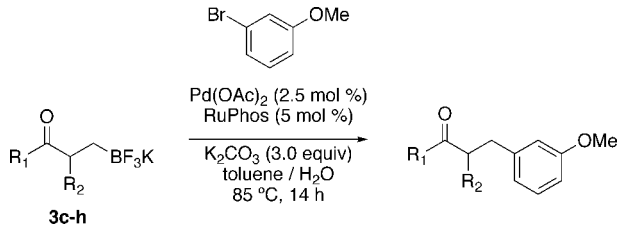
entry	electrophile	product	% isolated yield
1		 **8a**	trace
2		 **8b**	trace
3		 **8c**	74
4		 **8a**	68
5		 **8d**	72
6		 **8d**	75

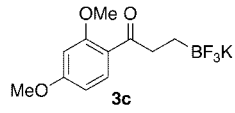
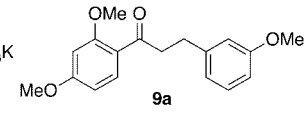
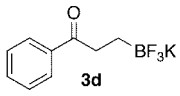
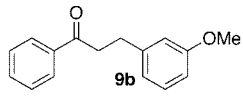
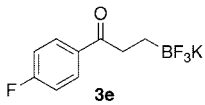
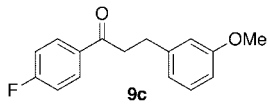
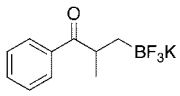
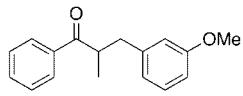
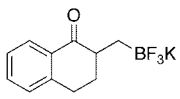
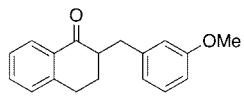
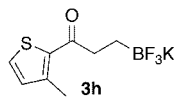
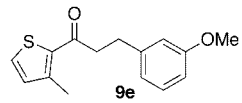
[a] All reactions were carried out using 0.25 mmol of the electrophile and 0.2525 mmol of potassium organotrifluoroborate **3g**.

Conclusion

In summary, we have prepared a variety of potassium trifluoroboratoketohomoenolates and shown that they are effective coupling partners in the Suzuki−Miyaura reaction. The ketone homoenolates are easily synthesized by either the conjugate addition of bis(pinacolato)diboron to α,β-unsaturated ketones or the alkylation of commercially available methyl ketones with iodomethylpinacolboronate. Aliphatic ketohomoenolates coupled efficiently with various types of aryl and heteroaryl chlorides in good to excellent yields. Aromatic ketohomoenolates were more difficult substrates to couple. The electron-poor aryl chlorides were the only chlorine-based electrophiles that cross-coupled in good yields, whereas both the electron-deficient and electron-rich aryl bromides were effective coupling partners. The cross-coupling of trifluoroboratohomoenolates provides a useful alternative to the Michael-type addition of organometallics to α,β-unsaturated enones, particularly in those cases where the desired nucleophilic component would require installation of sensitive functional groups that are incompatible with the organometallic being generated. Efforts

TABLE 7. Cross-Coupling of the Various Potassium Trifluoroboratohomoenolates with 3-Bromoanisole



entry	RBF_3K	product	% isolated yield
1	 **3c**	 **9a**	79
2	 **3d**	 **9b**	55
3	 **3e**	 **9c**	64
4	 **3f**	 **9d**	60
5	 **3g**	 **8a**	68
6	 **3h**	 **9e**	55

[a] All reactions were carried out using 0.25 mmol of the aryl bromide and 0.2525 mmol of potassium organotrifluoroborates.

toward the preparation and coupling of new potassium trifluoroboratohomoenolates are currently underway in our laboratory.

Experimental Section

Preparation of Potassium 1-Trifluoroborato-5-phenylpentan-3-one (3a). Strategy A. CuCl (51.3 mg, 0.52 mmol), sodium *tert*-butoxide (149.0 mg, 1.55 mmol), and DPEPhos (280.0 mg, 0.52 mmol) were combined in a flask, which was evacuated and filled with nitrogen. THF (16 mL) was added, and the mixture was stirred for 30 min at room temperature. A solution of bis(pinacolato)diboron (4.58 g, 18.0 mmol) in THF (16 mL) was added dropwise. Additional THF (8.0 mL) was used to rinse the flask containing the bis(pinacolato)diboron. The mixture was stirred for 30 min before cooling to 0 °C. At this point, 5-phenylpent-1-en-3-one (2.75 g, 17.2 mmol) in a solution of THF (8.0 mL) and methanol (1.3 mL) was successively added, and the mixture was stirred for 30 min at 0 °C followed by 2.5 h at room temperature. The resulting suspension was filtered through Celite, rinsing with EtOAc (3 × 10 mL). The filtrate was concentrated under reduced pressure, and the resulting oil was dissolved in MeCN (67 mL) and cooled to 0 °C. Saturated aqueous KHF_2 (4.5 M, 15 mL, 69.0 mmol) was added dropwise. The resulting suspension was stirred for 3 h, concentrated under reduced pressure, and then placed under high vacuum overnight. The crude product was then extracted with hot acetone (3 × 30 mL). The insoluble salts were filtered off, and the filtrate was concentrated in vacuo. Et_2O (50 mL) was added to the crude compound, and the suspension was sonicated for 30 min and then filtered to provide the desired trifluoroboratohomoenolate **3a** in 60% yield (2.8 g, 10.4 mmol). Mp = 205−210 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.26−7.13 (m, 5H), 2.7−2.68 (m, 4H), 2.14−2.10 (m, 2H), 0.14 (br s, 2H); ^{13}C NMR (125.8 MHz, DMSO-d_6) δ 213.3, 141.6, 128.14, 128.09, 125.6, 42.0, 40.0, 29.3; ^{19}F NMR (471 MHz, DMSO-d_6) δ −138.7 (m); ^{11}B NMR (128 MHz, DMSO-d_6) δ 4.7 (br s); IR (KBr) 2906, 1712, 960 cm^{-1}; HRMS (ES−) *m*/*z* calcd for $C_{11}H_{13}BF_3O$ (M − K$^+$) 229.1012, found 229.1015.

Preparation of Potassium 2-(Trifluoroboratomethyl)-3,4-dihydronaphthalene-1(2*H*)-one (3g). Strategy B. α-Tetralone (4.0 g, 27.4 mmol) was dissolved in THF (100 mL) and cooled to −78 °C in a CO_2(s)/acetone bath. A solution of LiHMDS (1.0 M in THF, 33.0 mL, 33.0 mmol) was added dropwise, and the resulting solution was stirred for 30 min. At this point, iodomethylpinacol boronate (11.0 g, 41.0 mmol) was added dropwise, and the mixture was stirred for an additional 30 min at −78 °C and then allowed to warm to room temperature for 2 h. The solution was then cooled to 0 °C, and pH 7 buffer (50 mL) was added dropwise. The resulting mixture was extracted with EtOAc (3 × 50 mL), and the organic phase was washed with saturated aqueous NaCl (30 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The resulting oil was dissolved in MeCN (110 mL) and cooled to 0 °C. Saturated aqueous KHF_2 (4.5 M, 25 mL, 110.0 mmol) was added dropwise, and the resulting suspension was stirred for 3 h, concentrated under reduced pressure, and then placed under high vacuum overnight. Et_2O (50 mL) was added to the crude compound, and the suspension was sonicated for 30 min and filtered to remove all of the organic impurities. This operation was repeated twice. The resulting solid was purified by continuous Soxhlet extraction with acetone (50 mL) for 12 h to provide the desired trifluoroboratohomoenolate **3g** in 75% yield (5.4 g, 20.6 mmol). Mp >215 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.82 (d, J = 7.5 Hz, 1H), 7.47−7.44 (m, 1H), 7.29−7.26 (m, 2H), 2.98−2.96 (m, 1H), 2.79−2.77 (m, 1H), 2.40−2.37 (m, 1H), 2.14−2.11 (m, 1H), 1.91−1.88 (m, 1H), 0.48−0.46 (m, 1H), 0.13−0.10 (m, 1H); ^{13}C NMR (125.8 MHz, DMSO-d_6) δ 202.8, 144.3, 132.4, 132.2, 128.6, 126.5, 126.0, 44.6, 28.3, 26.6; ^{19}F NMR (471 MHz, DMSO-d_6) δ −135.8 (m); ^{11}B NMR (128 MHz, DMSO-d_6) δ 4.6 (br s); IR (KBr) 2916, 1678, 956 cm^{-1}; HRMS (ES−) *m*/*z* calcd for $C_{11}H_{11}BF_3O$ (M − K$^+$) 227.0855, found 227.0852.

Representative Procedure for the Suzuki−Miyaura Cross-Coupling Reaction of Potassium Trifluoroboratohomoenolates and Aryl Electrophiles: Preparation of 1-(3,5-Dimethoxyphenyl)-5-phenylpentan-3-one (5f). To a mixture of potassium 1-trifluoroborato-5-phenylpentan-3-one (**3a**) (541.4 mg, 2.02 mmol), 1-chloro-3,5-dimethoxybenzene (344.3 mg, 2.0 mmol), K_2CO_3 (829.3 mg, 0.75 mmol), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), and RuPhos (46.7 mg, 0.1 mmol) under nitrogen was added toluene/H_2O (4:1, 10.0 mL). The reaction was heated at 85 °C with stirring under a nitrogen atmosphere for 14 h and then cooled to room temperature. A solution of pH 7 buffer (10.0 mL) was added, and the resulting mixture was extracted with EtOAc (3 × 6 mL). The organic layer was dried ($MgSO_4$) and then filtered. The solvent was removed in vacuo, and the crude product was purified by silica gel chromatography (elution with EtOAc/hexane 10:90) to afford the product as a colorless oil in 89% yield (528.1 mg, 1.77 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28−7.24 (m, 2H), 7.19−7.14 (m, 3H), 6.31−6.29 (m, 3H), 3.76 (s, 6H), 2.89 (t, J = 7.5 Hz, 2H), 2.82 (t, J = 7.3 Hz, 2H), 2.73−2.67 (m, 4H); ^{13}C NMR (125.8

MHz, $CDCl_3$) δ 209.2, 161.1, 143.7, 141.2, 128.7, 128.5, 126.3, 106.6, 98.3, 55.5, 44.7, 44.6, 30.3, 30.0; IR (neat) 2935, 1713, 1151 cm^{-1}; HRMS (ES+) *m*/*z* calcd for $C_{19}H_{23}O_3$ ($M + H^+$) 299.1647, found 299.1647.

Acknowledgment. This work was generously supported by the National Institutes of Health (General Medical Sciences) and Merck Research Laboratories. BASF is thanked for their donation of bis(pinacolato)diboron. We also acknowledge Frontier Scientific and Johnson Matthey for a donation of palladium catalysts and Professor Stephen L. Buchwald (MIT) for a sample of phosphine ligands.

Supporting Information Available: Experimental procedures, spectral characterization, and copies of ^1H, ^{13}C, ^{11}B, and ^{19}F NMR spectra for all compounds prepared by the method described. This material is available free of charge via the Internet at http://pubs.acs.org.

JO802453M