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

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Abstract

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

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homoenolate tautomerism that is often irreversible

(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 tin¹⁰ or boro¹¹ 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.

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,11c,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 trifluoroborato-homoenolates 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 trifluoroborato-ketohomoenolates and their coupling with a wide variety of aryl- and heteroaryl chlorides.

Results and Discussion

Initially, we prepared an array of potassium trifluoroborato-ketohomoenolates using two different procedures. First, aliphatic trifluoroborato-ketohomoenolates were generated via the conjugate addition of bis(pinacolato)diboron to unsaturated ketones as reported by Yun and coworkers.^{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 the ketones **2a–c** in good to excellent yields^{18,19} (Scheme 1).

With these α,β -unsaturated ketones in hand, organoboron reagents were then prepared according to the conditions of Yun and coworkers^{13a} by using a combination of CuCl, DPEPhos (Figure 1) and NaOt-Bu. The resulting pinacolboronates were subsequently converted to the corresponding potassium organotrifluoroborates by quenching with KHF₂ (Strategy A, eq 2, Table 1). The aliphatic trifluoroboratoketohomoenolates were obtained in good yields.

Strategy A

(2)

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 KHF₂ 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

(3)

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 (5 mol %) using K₂CO₃ as a base and a mixture of toluene/H₂O as the solvent system. All of the electrophiles gave rise to the 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)

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 derivatives 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, 7–8). 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 1–2). 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 3–4). Electron-deficient electrophiles were then utilized, and both the chloride and the bromide derivatives provided the desired product (Table 6, entries 5–6).

With these results in hand, we next cross-coupled aromatic trifluoroborato ketohomoenolates with 3-bromoanisole as the electrophile (Table 7). All of the ketohomoenolates coupled in

better yields 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 trifluoroboratothomoenolate and the aromatic derivatives toward diverse aromatic electrophiles, a result whose genesis is not easily understood.

Conclusion

In summary, we have prepared a variety of potassium trifluoroboratothomoenolates and shown that they are effective coupling partners in the Suzuki-Miyaura reaction. The ketone thomoenolates 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 thomoenolates coupled efficiently with various types of aryl and heteroaryl chlorides in good to excellent yields. Aromatic thomoenolates 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 trifluoroboratothomoenolates provides a useful alternative to the Michael-type of 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 toward the preparation and coupling of new potassium trifluoroboratothomoenolates 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 and evacuated and filled with nitrogen. THF (16 mL) was added and the mixture was stirred for 30 minutes at room temperature. A solution of bis(pinacolato)diboron (4.58 g, 18.0 mmol) in THF (16 mL) was added drop wise. Additional THF (8.0 mL) was used to rinse the flask containing the bis(pinacolato)diboron. The mixture was stirred for 30 minutes 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) were successively added, and the mixture was stirred for 30 minutes at 0 C followed by 2.5 h at room temperature. The resulting suspension was filtered through Celite, rinsing with EtOAc (310 mL). The filtrate was concentrated under reduced pressure and the resulting oil was dissolved in MeCN (67 mL) and cooled to 0 C. Sat aq KHF₂ (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*. Et₂O (50 mL) was added to the crude compound and the suspension was sonicated for 30 minutes and then filtered to provide the desired trifluoroboratothomoenolate **3a** in 60% yield (2.8 g, 10.4 mmol). mp = 205–210 C; ¹H-NMR (500 MHz, DMSO-*d*₆) 7.26–7.13 (m, 5H), 2.7–2.68 (m, 4H), 2.14–2.10 (m, 2H), 0.14 (br s, 2H); ¹³C-NMR (125.8 MHz, DMSO-*d*₆) 213.3, 141.6, 128.14, 128.09, 125.6, 42.0, 40.0, 29.3; ¹⁹F NMR (471 MHz, DMSO-*d*₆) -138.7 (m); ¹¹B NMR (128 MHz, DMSO-*d*₆) 4.7 (br s); IR (KBr) 2906, 1712, 960 cm⁻¹; HRMS (ES-) *m/z* calcd. for C₁₁H₁₃BF₃O (M-K⁺) 229.1012, found 229.1015.

Preparation of Potassium 2-(Trifluoroboratomethyl)-3,4-dihydronaphthalene-1(2H)-one (**3g**). Strategy B

α -Tetralone (4.0 g, 27.4 mmol) was dissolved in THF (100 mL) and cooled to $-78\text{ }^{\circ}\text{C}$ in a $\text{CO}_2(\text{s})/\text{acetone}$ 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 minutes. At this point, iodomethylpinacol boronate (11.0 g, 41.0 mmol) was added dropwise, and the mixture was stirred for an additional 30 minutes at $-78\text{ }^{\circ}\text{C}$ then allowed to warm to room temperature for 2 h. The solution was then cooled to $0\text{ }^{\circ}\text{C}$ and pH 7 buffer (50 mL) was added dropwise. The resulting mixture was extracted with EtOAc ($3 \times 50\text{ mL}$) and the organic phase was washed with sat aq NaCl (30 mL), dried (MgSO_4), and concentrated under reduced pressure. The resulting oil was dissolved in MeCN (110 mL) and cooled to $0\text{ }^{\circ}\text{C}$. Sat aq 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 minutes 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 trifluoroborato-homoenolate **3g** in 75% yield (5.4 g, 20.6 mmol). mp $> 215\text{ }^{\circ}\text{C}$; $^1\text{H-NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ 7.82 (d, $J = 7.5\text{ Hz}$, 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); $^{13}\text{C-NMR}$ (125.8 MHz, $\text{DMSO-}d_6$) δ 202.8, 144.3, 132.4, 132.2, 128.6, 126.5, 126.0, 44.6, 28.3, 26.6; $^{19}\text{F-NMR}$ (471 MHz, $\text{DMSO-}d_6$) δ -135.8 (m); $^{11}\text{B-NMR}$ (128 MHz, $\text{DMSO-}d_6$) δ 4.6 (br s); IR (KBr) 2916, 1678, 956 cm^{-1} ; HRMS (ES^-) m/z calcd. for $\text{C}_{11}\text{H}_{11}\text{BF}_3\text{O}$ (M-K^+) 227.0855, found 227.0852.

Representative Procedure for the Suzuki-Miyaura Cross-Coupling Reaction of Potassium Trifluoroborato-homoenolates 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), $\text{Pd}(\text{OAc})_2$ (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 $85\text{ }^{\circ}\text{C}$ with stirring under a nitrogen atmosphere for 14 h and then cooled to rt. A solution of pH 7 buffer (10.0 mL) was added, and the resulting mixture was extracted with EtOAc ($3 \times 6\text{ mL}$). 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). $^1\text{H-NMR}$ (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, $J = 7.5\text{ Hz}$, 2H), 2.82 (t, $J = 7.3\text{ Hz}$, 2H), 2.73–2.67 (m, 4H); $^{13}\text{C-NMR}$ (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 $\text{C}_{19}\text{H}_{23}\text{O}_3$ ($\text{M}+\text{H}^+$) 299.1647, found 299.1647.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgment

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

FIGURE 1.
DPEPhos ligand

RuPhos

FIGURE 2.
RuPhos ligand

R = alkyl, Ar

quantitative over
the two steps¹⁸

SCHEME 1.

TABLE 1

Preparation of Potassium Trifluoroborato ketohomoenolates 3a–h

entry

reactant

1

entry

reactant

2

entry

reactant

3

entry

reactant

4

entry

reactant

5

6

entry

reactant

7

29

entry

reactant

8

2h

entry**reactant**

^a Starting methyl ketones were freshly distilled from commercial sources.

^b Strategy A: B₂Pin₂ (1.5 equiv), 3% CuCl, 3% DPEPhos, 9% NaO*t*-Bu, THF/MeOH, 3 h, then KHF₂ (aq); yield after four steps.

^c Strategy B: ICH₂BPIn (1.5 equiv), LHMDs (1.2 equiv), THF, 2.5 h, then KHF₂ (aq); yield after two steps.

TABLE 2

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

entry	aryl chloride		3a Pd(OAc) ₂ (2.5 mol %) RuPhos (5 mol %) K ₂ CO ₃ (3.0 equiv) toluene / H ₂ O 85 °C, 14 h
1
2

3a
Pd(OAc)₂ (2.5 mol %)
RuPhos (5 mol %)
K₂CO₃ (3.0 equiv)
toluene / H₂O
85 °C, 14 h

entry

aryl chloride

3

PI

3aPd(OAc)₂ (2.5 mol %)
RuPhos (5 mol %)K₂CO₃ (3.0 equiv)
toluene / H₂O
85 °C, 14 h

entry

aryl chloride

4

5

3a
Pd(OAc)₂ (2.5 mol %)
RuPhos (5 mol %)
K₂CO₃ (3.0 equiv)
toluene / H₂O
85 °C, 14 h

entry

aryl chloride

6

3a
Pd(OAc)₂ (2.5 mol %)
RuPhos (5 mol %)
K₂CO₃ (3.0 equiv)
toluene / H₂O
85 °C, 14 h

entry

aryl chloride

7

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

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

entry	aryl chloride	<div><div> </div><div>3a Pd(OAc)₂ (2.5 mol %) RuPhos (5 mol %) K₂CO₃ (3.0 equiv) toluene / H₂O 85 °C, 14 h</div></div>	
1

3a
Pd(OAc)₂ (2.5 mol %)
RuPhos (5 mol %)
K₂CO₃ (3.0 equiv)
toluene / H₂O
85 °C, 14 h

entry

aryl chloride

2

3a
Pd(OAc)₂ (2.5 mol %)
RuPhos (5 mol %)
K₂CO₃ (3.0 equiv)
toluene / H₂O
85 °C, 14 h

entry

aryl chloride

3

4

3a
Pd(OAc)₂ (2.5 mol %)
RuPhos (5 mol %)
K₂CO₃ (3.0 equiv)
toluene / H₂O
85 °C, 14 h

entry

aryl chloride

5

3a
Pd(OAc)₂ (2.5 mol %)
RuPhos (5 mol %)
K₂CO₃ (3.0 equiv)
toluene / H₂O
85 °C, 14 h

entry

aryl chloride

6

3a
Pd(OAc)₂ (2.5 mol %)
RuPhos (5 mol %)
K₂CO₃ (3.0 equiv)
toluene / H₂O
85 °C, 14 h

entry

aryl chloride

7

^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

		HetArCl	3a Pd(OAc) ₂ (2.5 mol %) RuPhos (5 mol %) K ₂ CO ₃ (3.0 equiv) toluene / H ₂ O 85 °C, 14 h
entry	heteroaryl chloride		
1
2

entry

heteroaryl chloride

3

entry

heteroaryl chloride

4

		3a Pd(OAc) ₂ (2.5 mol %) RuPhos (5 mol %) HetArCl K ₂ CO ₃ (3.0 equiv) toluene / H ₂ O 85 °C, 14 h
entry	heteroaryl chloride	
5

entry

heteroaryl chloride

6

		3a Pd(OAc) ₂ (2.5 mol %) RuPhos (5 mol %) HetArCl K ₂ CO ₃ (3.0 equiv) toluene / H ₂ O 85 °C, 14 h	
entry	heteroaryl chloride		
7			P
8			P

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

TABLE 5

Cross-Coupling of Various Potassium Organotrifluoroboratoenolates with 5-Chloro-1,3-Dimethoxybenzene

entry

 RBF_3K

1

2

entry

3

3c

4

3d

5

3e

RBF₃K

entry

RBF₃K

6

entry

 RBF_3K

7

entry

RBF₃K

8

^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 %), RuPhos (10 mol %) were used.

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

J Org Chem. Author manuscript; available in PMC 2010 February 6.

entry

electrophile

4

5

entry

electrophile

6

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

TABLE 7

Cross-Coupling of the Various Potassium Organotrifluoroboratoenolates with 3-Bromoanisole

	$\text{Pd}(\text{OAc})_2$ (2.5) RuPhos (5 m)
	K_2CO_3 (3.0 e toluene / H 85 °C, 14

	3c-h

entry

 RBF_3K

1

Pd(OAc)₂ (2.5)
RuPhos (5 m

K₂CO₃ (3.0 e
toluene / H
85 °C, 14

3c-h

entry

RBF₃K

2

3d

$\text{Pd}(\text{OAc})_2$ (2.5)
 RuPhos (5 m)

K_2CO_3 (3.0 e)
toluene / H
85 °C, 14

3c-h

entry

RBF_3K

3

Pd(OAc)₂ (2.5
RuPhos (5 m

K₂CO₃ (3.0 e
toluene / H
85 °C, 14

3c-h

entry

RBF₃K

4

3f

$\text{Pd}(\text{OAc})_2$ (2.5)
 RuPhos (5 m)

K_2CO_3 (3.0 e
toluene / H
85 °C, 14

3c-h

entry

RBF_3K

5

3g

Pd(OAc)₂ (2.5)
RuPhos (5 m

K₂CO₃ (3.0 e
toluene / H
85 °C, 14

3c-h

entry

RBF₃K

6

3h

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