Tetrahedron Letters 52 (2011) 1008-1010

Contents lists available at ScienceDirect

**Tetrahedron Letters** 

journal homepage: www.elsevier.com/locate/tetlet

# Palladium-catalyzed direct cross-coupling of potassium styryltrifluoroborates and benzoyl chlorides—a one step method for chalcone synthesis

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### ARTICLE INFO

## ABSTRACT

heating is developed.

Article history: Received 20 November 2010 Revised 10 December 2010 Accepted 19 December 2010 Available online 24 December 2010

Keywords: Cross-coupling Benzoyl chlorides Potassium styryltrifluoroborates Microwave heating

Potassium organotrifluoroborates are new organometallic reagents in organic synthesis. They are versatile, non-toxic, insensitive to moisture and air, and have long shelf lives.<sup>1</sup> Potassium organotrifluoroborates are interesting boron reagents for crosscoupling chemistry. While investigating the palladium-catalyzed direct cross-coupling reaction of benzoyl chlorides and potassium styryltrifluoroborates, we found that Stille<sup>2</sup> successfully developed the direct cross-coupling reaction of organotin compounds and acid chlorides for ketone synthesis. Several others have also reported a similar cross-coupling reaction by using arylboronic acids

A direct cross-coupling reaction of benzoyl chlorides and potassium styryltrifluoroborates to the corre-

sponding  $\alpha$ , $\beta$ -unsaturated aromatic ketones in the presence of PdCl<sub>2</sub>(d<sup>4</sup>bpf) catalyst under microwave



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<sup>0040-4039/\$ -</sup> see front matter  $\odot$  2010 Elsevier Ltd. All rights reserved. doi:10.1016/j.tetlet.2010.12.085

and acid chlorides as starting reagents.<sup>3</sup> Except for those reports there is no other example involving the direct oxidative addition of benzoyl chloride to a palladium(0) complex yielding ArCO-Pd-X and cross-coupled with potassium styryltrifluoroborate. In this communication, we report for the first time the successful microwave irradiated palladium-catalyzed direct cross-coupling reaction of benzoyl chlorides and potassium styryltrifluoroborates to the corresponding  $\alpha$ , $\beta$ -unsaturated aromatic ketones (Scheme 1).

Optimal conditions leading to the formation of  $\alpha$ , $\beta$ -unsaturated aromatic ketones **3** from the Pd-catalyzed cross-coupling reactions of potassium styryltrifluoroborates **1** and benzoyl chlorides **2** are summarized in Table 1. The formation of 1,3-diarylpropenone **3b** from the cross-coupling of potassium styryltrifluoroborate **1b** and benzoyl chloride **2b** was shown as a representative procedure. 0.5 mmol (1 equiv) of Potassium styryltrifluoroborate **1b** was reacted with 1.0 mmol (2 equiv) of benzoyl chloride **2b** along with 0.5 mmol of K<sub>2</sub>CO<sub>3</sub>, 1.5 mol % of PdCl<sub>2</sub>(d<sup>r</sup>bpf) catalyst, and a magnetic bar in a microwave tube. The reactants were then flushed with argon for 1–2 min to prevent the presence of air from causing

the decomposition of the Pd-catalyst followed by the addition of 2.0 mL of dry 1,4-dioxane from a sure-seal bottle. The resulting mixture in the microwave tube was subsequently inserted into the microwave and heated at 140 °C for 30 min at 300 W. After removal from the microwave, the product mixture was extracted with diethyl ether and separated from the inorganic byproducts through filtration. The crude product was subjected to silica gel chromatography with hexane/ethyl acetate (25:1) as the eluent and the pure product **3b** was isolated, dried, and characterized by GC-MS and NMR. To observe the sensitivity of the substituent on the aromatic ring of the potassium arylvinyltrifluoroborates, groups attached to the aryl rings, such as CH<sub>3</sub>, CF<sub>3</sub>, and Cl were introduced and the corresponding cross-coupling  $\alpha,\beta$ -unsaturated aromatic ketones were obtained in high yields (Table 1, entries 1, 3, 5, 7).<sup>4</sup> Under the present reaction condition, benzoyl bromide gave a homo-coupling diketone product as the major product along with very little cross-coupling product. But benzovl chlorides with various substituents in the aromatic rings worked efficiently (Table 1, entries 1-8). Cross-coupling reaction of styryltrifluoroborates

Table 1

Pd-catalyzed cross-coupling reaction of potassium styryltrifluoroborates and benzoyl chlorides<sup>a</sup>



<sup>a</sup> All products were purified by subjecting to silica gel chromatography using hexane/ethyl acetate as eluents.





with acylating agents such as, phenyl acetyl chloride and acetic anhydride were attempted but no significant progress was obtained.

So far, it appears that utilizing 1,4-dioxane as the solvent system resulted in successful cross-coupling product formation. Although 1,4-dioxane is a non-polar solvent not typically used for microwave reactions, the polarizability of the two oxygen and the relatively high boiling point provided favorable conditions for cross-coupling to occur. Changing molar ratios of the reagents, changing the palladium complex, ligand, increasing amount of Pd-catalyst, and changing the amount of potassium carbonate base had no effect in an isopropanol/H<sub>2</sub>O or 100% isopropanol solvent system.<sup>5</sup>

A mechanism for the direct cross-coupling reaction of potassium styryltrifluoroborates and benzoyl chlorides is proposed in Scheme 2. The catalytic cycle involves the palladium inserted nucleophilic species of benzoyl chloride by oxidative addition followed by ligand exchange with the base,  $K_2CO_3$ . The transmetallation of the organoboron species to the organopalladium species subsequently occurs, followed by the formation of the desired  $\alpha,\beta$ -unsaturated ketone by reductive elimination and the re-generation of palladium catalyst.

In conclusion, we were able to report the development of a new palladium catalyst system allowing the successful cross-coupling reactions of potassium styryltrifluoroborates and benzoyl chlorides, furnishing  $\alpha$ , $\beta$ -unsaturated aromatic ketones or chalcones in a single step process under microwave heating. The procedure possesses several advantages over similar reactions such as the fact that potassium styryltrifluoroborates are easy to prepare, nontoxic, and easily removable. Further use of these developments in synthetic organic chemistry is in progress.

## Acknowledgments

Financial support from US department of education Title III Grant, Tennessee State University is thankfully acknowledged.

## Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.12.085.

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- Spectral data of new compounds: Compound 3a: LRMS: Calculated for  $C_{17}H_{16}O_2 M^+$  252. Found: 252. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  7.96–6.88 (m, 10H, Aromatic), 3.79 (s, 3H, OCH<sub>3</sub>), 2.30 (s, 3H, CH<sub>3</sub>);  $^{13}$ C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$ 188.7, 144.0, 140.7, 131.1, 129.6, 128.3, 120.7, 113.7, 55.4, 21.4. Compound 3c: LRMS: Calculated for  $C_{17}H_{13}F_{3}O$  M<sup>+</sup> 290. Found: 292 (M+2). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.06–7.31(m, 8H, aromatic), 7.79 (d, J = 15.6 Hz, 1H), 7.61 (d, J = 15.6 Hz, 1H), 2.47 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (CDCI<sub>3</sub>, 75.5 MHz) δ 189.4, 162.5, 145.5, 135.1, 130.6, 128.6, 125.9, 124.1, 21.8; <sup>19</sup>F NMR (CDCI<sub>3</sub>, 282.3 MHz) δ -63.2. Compound **3e**: LRMS: Calculated for C<sub>16</sub>H<sub>9</sub>F<sub>3</sub>Cl<sub>2</sub>O M<sup>+</sup> 244. Found: 246. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.09–7.47 (m, 6H, aromatic), 7.76 (d, J = 21.0 Hz, 1H), NMR (CDCl<sub>3</sub>, 560 MHz)  $\delta$  360 MHz)  $\delta$  360 MHz)  $\delta$  360 MHz)  $\delta$  375 MHz)  $\delta$  187.4, 164.6, 143.8, 137.3, 133.3, 131.3, 130.4, 128.8, 127.4, 122.8; <sup>19</sup>F NMR (CDCl<sub>3</sub>, 282.3 MHz)  $\delta$  -63.2 (CF<sub>3</sub>). Compound **3g**: LRMS: Calculated for C<sub>15</sub>H<sub>10</sub>FCIO M<sup>+</sup> 260. Found: 262. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 7.83–6.84 (m, 10H, Aromatic); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  188.3, 143.4, 131.3, 131.0, 129.2, 121.7, 115.8;  $^{19}{\rm F}$  NMR (CDCl<sub>3</sub>, 282.3 MHz) –102.4 (F). Compound **3h**: LRMS: Calculated for C<sub>16</sub>H<sub>11</sub>F<sub>3</sub>O M<sup>+</sup> 276. Found: 276. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 8.11–7.43 (m, 10H, Aromatic), 7.74 (d, J = 15.9 Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz)  $\delta$  199.9, 158.9, 142.7, 134.4, 130.4, 128.7, 125.7, 31.5; <sup>19</sup>F NMR (CDCl<sub>3</sub>, 282.3 MHz)  $\delta$  –63.2 (CF<sub>3</sub>).
- 5. No cross-coupling product was obtained in iso-propanol or iso-propanol/water.