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Rhodium(III)-Catalyzed β-Arylation and -Alkenylation of α-Trifluoromethylacrylic Acid

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Rhodium(III)-Catalyzed β-Arylation and -Alkenylation of α-Trifluoromethylacrylic Acid

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The β-arylation and -alkenylation of trifluoromethylacrylic acid with arylboronic acids and alkenes proceed smoothly under rhodium(III) catalysis. The procedures provide useful synthetic routes from readily available building brocks to β-aryl-α-trifluoromethylpropanoic acid and 5,5,5-trifluoro-1,3-butadiene derivatives. Some of obtained butadienes exhibit strong fluorescence in the solid state. Keywords: rhodium catalyst; arylation, alkenylation, organofluorine compound

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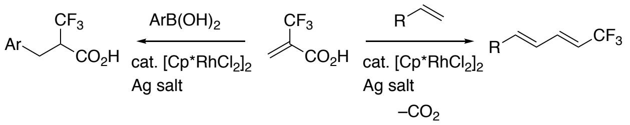
Organofluorine compounds are of importance in pharmaceutical, agrochemical, and polymer industries as well as in material sciences.[1] Trifluoromethyl group is the most fundamental fluorine-containing unit, which can be seen in a wide range of fine chemicals. The introduction of trifluoromethyl group into organic molecules[2] can influence the electron distribution and lipophilicity of parent molecules to enhance biological and physical properties.[3] Among such trifluoromethyl-substituted molecules, β-aryl-α-trifluoromethylpropanoic acids have attracted attention because of their biological activities and utilities as important synthetic intermediates in fine chemicals producing processes.[4] For preparing the class of compounds, nucleophilic and electrophilic trifluoromethylation reactions of α-activated carbonyl compounds have been developed. For example, Hu and co-workers reported copper-mediated nucleophilic trifluoromethylation of α-diazo esters with $TMSCF_3$.[5] As an electrophilic reagent, Poisson, Besset, and co-workers used Togni's reagent in their NHC carbene-catalyzed trifluoromethylation of α-chloroaldehydes.[6] In these precedents, however, reactive substrates and/or reagents have to be employed for preparing desired β-aryl-α-trifluoromethylpropanoic acids efficiently. An alternative is to utilize stable, readily available building blocks containing a trifluoromethyl group.[7] We focused attention on commercially available α-trifluoromethylacrylic acid. The catalytic coupling of this substrate can provide straightforward synthetic routes to trifluoromethyl-containing compounds. In the context of our continuous studies of rhodium(III)-catalyzed coupling reactions,[8] we found that α-trifluoromethylacrylic acid undergoes β-arylation upon treatment with arylboronic acids under rhodium(III) catalysis to produce β-aryl-α-trifluoromethylpropanoic acids[9] (Scheme 1). This type of 1,4-conjugate addition of arylboron reagents toward α,β-unsaturated carboxylic acids and related compounds has been conducted mainly under palladium(II)-, rhodium(I)-, or ruthenium(II) catalysis.[10] In contrast, the rhodium(III)-catalyzed version has been less explored. In addition, the rhodium(III)-catalyzed oxidative coupling of this building block with alkenes was also examined. Fortunately, we succeeded in finding that the β-alkenylation proceeds through C–H bond cleavage[11] and decarboxylation[12,13] to produce 5,5,5-trifluoro-1,3-butadiene derivatives. These new findings are described herein.

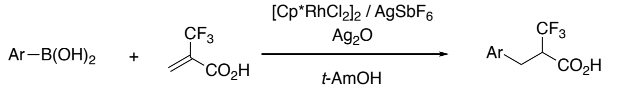


Scheme 1.

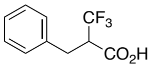
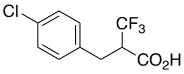
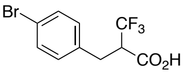
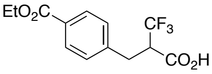
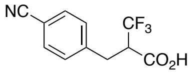
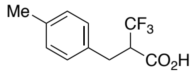
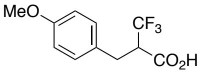
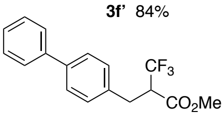
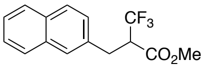
In an initial attempt, phenylboronic acid (**1a**) (1 mmol) was treated with α-trifluoromethylacrylic acid (**2**) (0.5 mmol) in the presence of $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (0.02 mmol, 4 mol% Rh), Ag_2O (1 mmol), and PivOH (0.5 mmol) under argon in *t*-AmOH (3 mL) at 50 °C for 20 h. After subsequent methyl-esterification using methyl iodide (2.5 mmol) and K_2CO_3 (1.5 mmol) in DMF at rt, methyl 2-benzyl-3,3,3-trifluoropropanate (**3a**) was formed as a 1,4-conjugate addition product in 72% yield (entry 1 in Table S1). Under optimal conditions using $[Cp^*RhCl_2]_2$ (0.01 mmol), $AgSbF_6$ (0.1 mmol), and Ag_2O (1 mmol), **3a** was produced in 95% yield (entry 15 in Table S1).[14] The volatility of ester **3a** made the posttreatment difficult. Fortunately, the corresponding acid, 2-benzyl-3,3,3-trifluoropropanoic acid (**3a'**), could be obtained in 93% isolated yield by avoidance of the methyl-esterification procedure (Table 1). It was confirmed that the present reaction can be readily scaled up. Thus, **3a** was obtained in 75% isolated yield (813 mg) from **1a** (10 mmol) and **2** (5 mmol) (entry 16 in Table S1).

Under the optimized conditions (entry 15 in Table S1), we next examined the reactions of variously substituted phenylboronic acids **1** with **2**. (Table 1). Electron-withdrawing (-Cl (**2b**), -Br (**2c**), $-CO_2Et$ (**2d**), and -CN (**2e**)) and -donating groups (-Me (**2f**) and -OMe (**2g**)) were tolerated to give the corresponding β-phenyl-α-trifluoromethylpropanoic acids **3b'-g'** in 51-92% yields. In cases using 4-biphenyl- (**2h**) and 2-naphthylboronic acids (**2i**), products **3'** were found to be sparingly soluble in common organic solvents. Therefore, they were treated with MeI and K_2CO_3 to make posttreatment easy. Thus, methyl esters **3h** and **3i** were obtained in 73 and 50% isolated yields, respectively.

Table 1. Reaction of Arylboronic Acids **1** with α-Trifluoromethylacrylic Acid (**2**)[a]

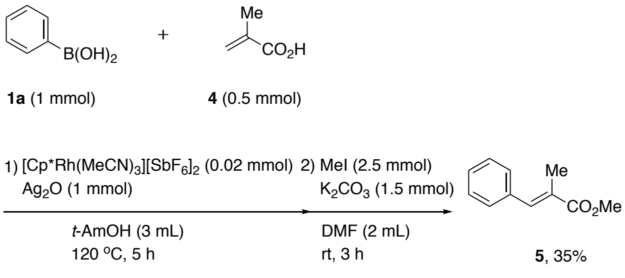


1 **2** **3**

product	yield (%)
 **3a'**	93%
 **3b'**	84%
 **3c'**	88%
 **3d'**	92%
 **3e'**	51%
 **3f'**	84%
 **3g'**	75%
 **3h**	73%[b]
 **3i**	50%[b]

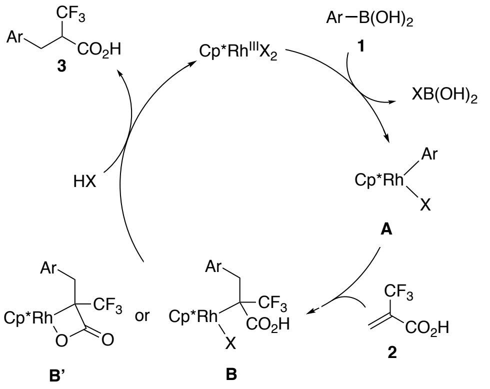
[a] Reaction conditions: **1** (1 mmol), **2** (0.5 mmol), $[Cp^*RhCl_2]_2$ (0.01 mmol), $AgSbF_6$ (0.1 mmol), Ag_2O (1 mmol), in t-AmOH (3 mL) under Ar at 50 °C for 20 h, unless otherwise noted. [b] Isolated as a methyl ester after treatment with MeI (2.5 mmol), K_2CO_3 (1.5 mmol) and DMF (2 mL) at rt for 2 h.

In contrast to trifluoromethylacrylic acid **2**, methacrylic acid (**4**) underwent Mizoroki-Heck type reaction upon treatment with **1a** under the present conditions (Scheme 2). After the methyl-esterification, methyl (*E*)-2-methyl-3-phenylacrylate (**5**) was formed selectively, albeit with a low yield. Unexpectedly, no 1,4-conjugate addition product was detected at all.



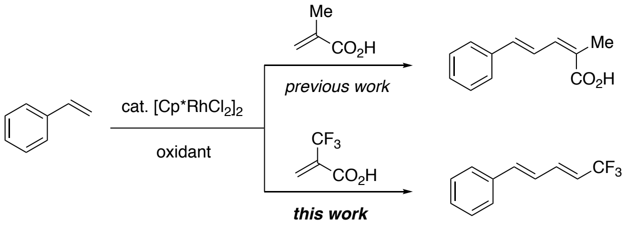
Scheme 2.

A plausible mechanism for the 1,4-conjugate addition of arylboronic acid **1** to α-trifluoromethylacrylic acid (**2**) is shown in Scheme 3. First, a Cp*-rhodium(III) species undergoes transmetalation with **1** to form an arylrhodium intermediate **A**. Then, **A** may undergo the insertion of **2** into its Ar–Rh bond to form a rhodium enolate intermediate **B**. Only a *C*-bonded tautomer is depicted in the scheme for clarity. The carboxylic group in **B** seems to be more acidic for the electron-withdrawing effect of its CF_3 group compared to that in the corresponding intermediate in the reaction of methacrylic acid (**4**). Therefore, the carboxylate moiety can readily coordinate to the rhodium center to form **B'**, which may show resistance to undergoing β-hydrogen elimination.[15] Finally, hydrolysis of **B** or **B'** appears to take place to selectively produce **3** and to regenerate an active Cp*-rhodium(III) species. It is also possible that the hydrolysis step proceeds more smoothly in the presence of acidic **2**, compared to that in the case with **4**.



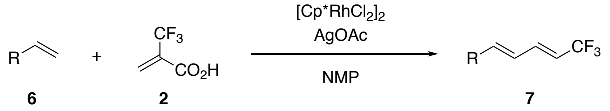
Scheme 3.

Next, the alkenylation of α-trifluoromethylacrylic acid (**2**) was examined. Previously, we reported that methacrylic acid (**4**) undergoes β-alkenylation upon treatment with alkenes such as styrene in the presence of Cp*-rhodium(III) catalyst and cupper salt oxidant (Scheme 4).[13] Under similar conditions, **2** reacted with styrene (**6a**) accompanied by decarboxylation[16] to produce ((1*E*,3*E*)-5,5,5-trifluoropenta-1,3-dien-1-yl)benzene (**7a**) selectively, albeit with a low yield (entry 1 in Table S2). In contrast to the case with **4**, by-products possessing a carboxylic group could not be detected. The yield of **7a** was enhanced to 46% by using AgOAc as oxidant in NMP (Table 2, entry 11 in Table S2). In most cases, small amounts (<5%) of geometric isomer(s) were detected. It should be noted that trifluoromethyl-capped phenylbutadiene derivatives are of interest for their physical properties and their reactivity.[17] 4-Methyl (**6b**) and -chlorostyrenes (**6c**) also coupled with **2** under similar conditions to give **7b** and **7c** in moderate yields. The reactions of 4-vinyl-1,1'-biphenyl (**6d**) and 2-vinylnaphthalene (**6e**) could be conducted in a similar manner to yield **7d** and **7e**. Butyl (**6f**) and Octyl acrylates (**6g**) also underwent decarboxylative coupling with **2** to produce the corresponding (2*E*,4*E*)-6,6,6-trifluorohexa-2,4-dienoates **7f** and **7g**. In the cases using acrylates, the use of twice amount of rhodium catalyst gave better results.

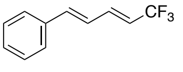


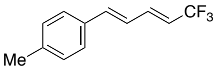
Scheme 4.

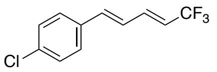
Table 2. Reaction of α-Trifluoromethylacrylic Acid (**2**) with Alkenes **6**[a]

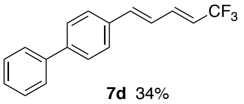


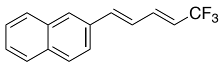
product yield (%)

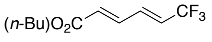

7a 46%

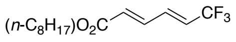

7b 40%


7c 41%


7d 34%


7e 40%


7f 40%[b]


7g 39%[b]

[a] Reaction conditions: **6** (2 mmol), **2** (0.5 mmol), $[Cp^*RhCl_2]_2$ (0.005 mmol), AgOAc (1 mmol) in NMP (2.5 mL) under Ar at 120 °C for 6 h, unless otherwise noted. [b] $[Cp^*RhCl_2]_2$ (0.01 mmol) was used.

Finally, we conducted preliminary investigations on the properties of prepared trifluoromethyl-capped butadienes. Compounds **7d** and **7e** showed strong fluorescence in the solid state at 383 and 395 nm (excited at 310 nm) (Figure 1). The quantum efficiency of the solid-state fluorescence was determined to be absolute values of 0.30 and 0.29, respectively.

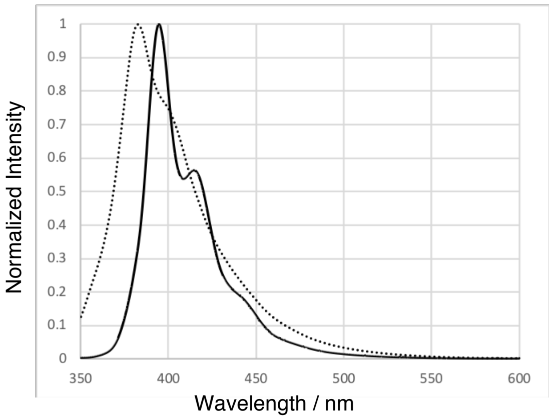


Figure 1. Normalized photoluminescence spectra (excited at 310 nm) of **7d** (dotted line) and **7e** (solid line) in solid state.

In summary, we have demonstrated that the β-arylation of readily available α-trifluoromethylacrylic acid can be achieved upon treatment with arylboronic acids in the presence of a rhodium(III) catalyst and a silver salt additive. Obtained β-aryl-α-trifluoromethylpropanoic acids are of interest because of their biological activities and utilities as important synthetic intermediates in fine chemicals producing processes. Moreover, it has been found that α-trifluoromethylacrylic acid also undergoes β-alkenylation under similar conditions accompanied by decarboxylation to produce trifluoromethyl-capped butadienes. Some of the latter products exhibit intense fluorescence in the solid state.

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Supporting Information is available electronically on J-STAGE.

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