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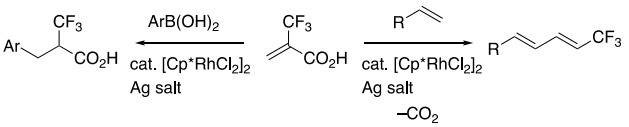
(Received <Month> <Date>, <Year>; CL-<No>; E-mail: <insert corresponding e-mail address>)

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

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.

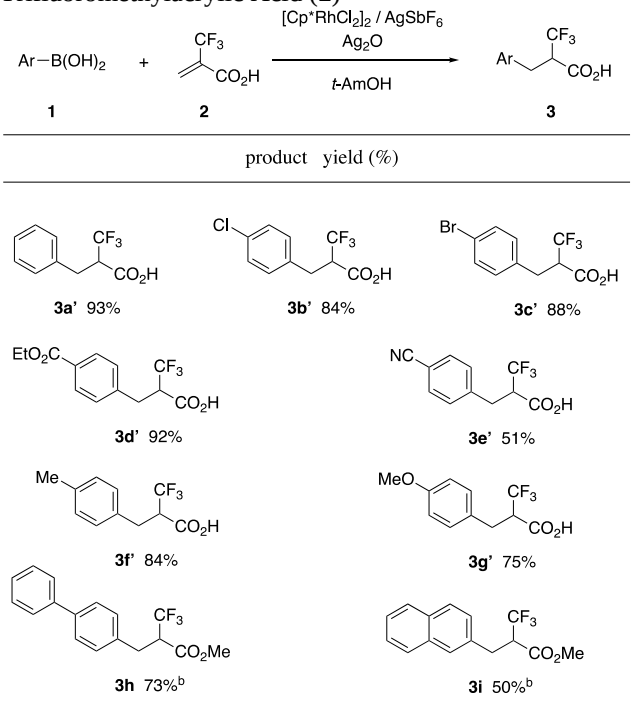


Scheme 1.

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).

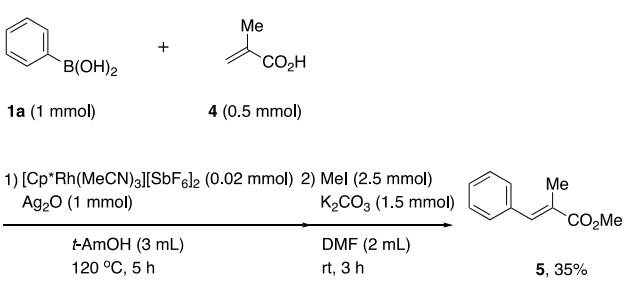
Under the optimized conditions (entry 15 in Table S1), we next examined the reactions of variously substituted phenylboronic acids **1** with **2**. (Table 1). Electron-withdrawing (-Cl (**2b**), -Br (**2c**), $-CO_2Et$ (**2d**), and -CN (**2e**)) and -donating groups (-Me (**2f**) and -OMe (**2g**)) 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]



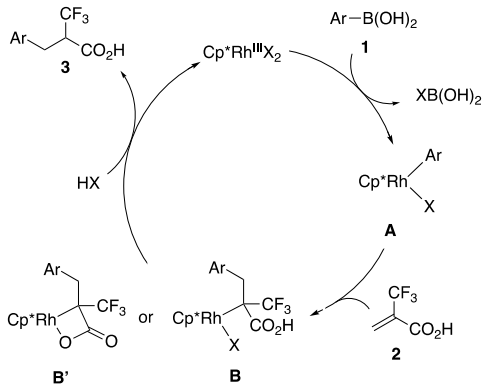
[a] Reaction conditions: **1** (1 mmol), **2** (0.5 mmol), $[Cp^*RhCl_2]_2$ (0.01 mmol), $AgSbF_6$ (0.1 mmol), Ag_2O (1 mmol), in *t*-AmOH (3 mL) under Ar at 50 °C for 20 h, unless otherwise noted. [b] Isolated as a methyl ester after treatment with MeI (2.5 mmol), K_2CO_3 (1.5 mmol) and DMF (2 mL) at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



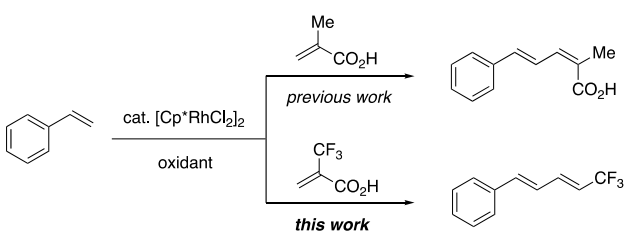
Scheme 2.

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**.



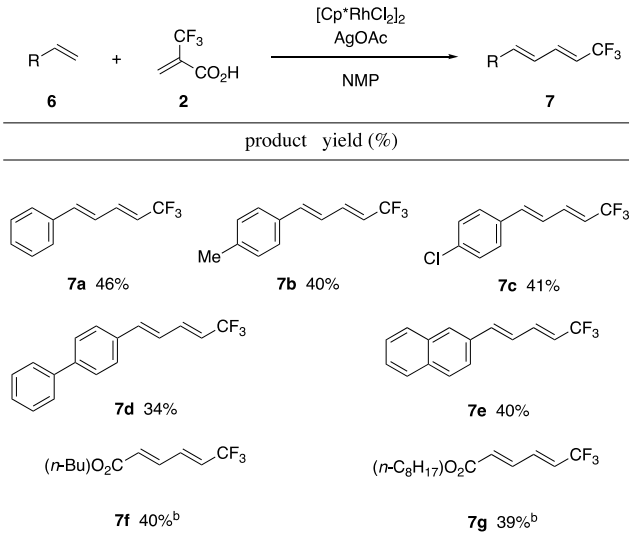
Scheme 3.

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]



[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.

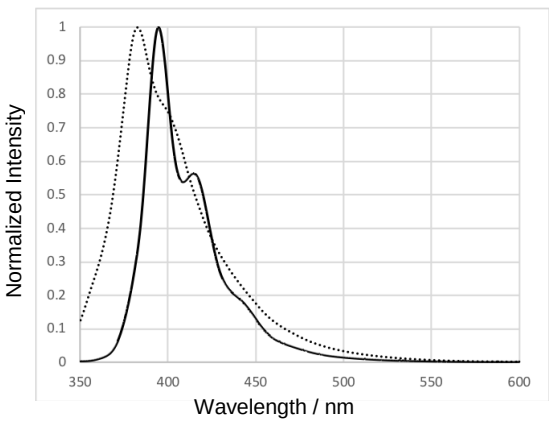


Figure 1. Normalized photoluminescence spectra (excited at 310 nm) of **7d** (dotted line) and **7e** (solid line) in solid state.

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.

This work was partly supported by JSPS KAKENHI Grant Numbers 18H04267 (in Precisely Designed Catalysts with Customized Scaffolding) and 18K19083 (Grant-in-Aid for Challenging Research (Exploratory)), Nagase Science Technology Foundation, and Yamada Science Foundation to T.S. and JSPS KAKENHI Grant Number JP18H04627 (in Frontier Research on Chemical Communications) to Y.U. We also thank Prof. Dr. N. Tohnai (Osaka University) for fluorescence quantum efficiency measurements and helpful discussions.

Supporting Information is available electronically on J-STAGE.

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Title(required)	Rhodium(III)-Catalyzed β-Arylation and -Alkenylation of α-Trifluoromethylacrylic Acid
Authors' Names(required)	Risa Yoshimoto , Yoshinosuke Usuki, and Tetsuya Satoh

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