

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

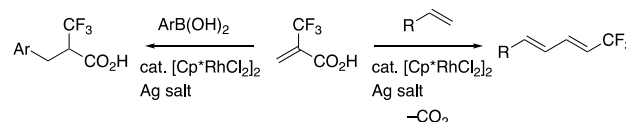
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The β -arylation and -alkenylation of trifluoromethylacrylic acid with arylboronic acids and alkenes proceed smoothly under rhodium(III) catalysis. The procedures provide useful synthetic routes from readily available building blocks to β -aryl- α -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

C–H bond cleavage¹¹ and decarboxylation^{12,13} to produce 5,5,5-trifluoro-1,3-butadiene derivatives. These new findings are described herein.



Scheme 1.

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 molecules² 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 TMSCF₃.⁵ 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 acids⁹ (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

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][SbF₆]₂ (0.02 mmol, 4 mol% Rh), Ag₂O (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 K₂CO₃ (1.5 mmol) in DMF at rt, methyl 2-benzyl-3,3,3-trifluoropropanoate (**3a**) was formed as a 1,4-conjugate addition product in 72% yield (entry 1 in Table S1). Under optimal conditions using [Cp*RhCl₂]₂ (0.01 mmol), AgSbF₆ (0.1 mmol), and Ag₂O (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).

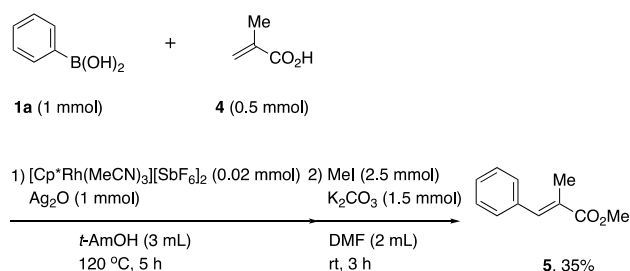
Under the optimized conditions (entry 15 in Table S1), we next examined the reactions of variously substituted phenylboronic acids **1** with **2**. (Table 1). Electron-withdrawing (-Cl (**2b**), -Br (**2c**), -CO₂Et (**2d**), and -CN (**2e**)) and -donating groups (-Me (**2f**) and -OMe (**2g**)) were 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 K₂CO₃ 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

$\text{Ar}-\text{B}(\text{OH})_2 + \text{CF}_3\text{CH}=\text{CHCO}_2\text{H} \xrightarrow[\text{t-AmOH}]{[\text{Cp}^*\text{RhCl}_2]_2 / \text{AgSbF}_6, \text{Ag}_2\text{O}}$		$\text{Ar}-\text{CH}(\text{CF}_3)\text{CH}_2\text{CO}_2\text{H}$
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

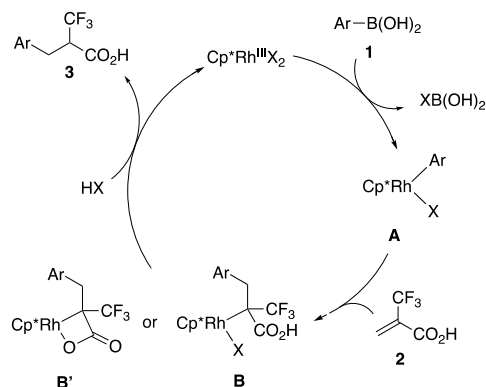
^a Reaction conditions: **1** (1 mmol), **2** (0.5 mmol), [Cp*RhCl₂]₂ (0.01 mmol), AgSbF₆ (0.1 mmol), Ag₂O (1 mmol), in *t*-AmOH (3 mL) under Ar at 50 °C for 20 h, unless otherwise noted. ^b Isolated as a methyl ester after treatment with MeI (2.5 mmol), K₂CO₃ (1.5 mmol) and DMF (2 mL) at rt for 2 h.

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 CF₃ 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 copper salt oxidant (Scheme 4).¹³ Under similar conditions, **2** reacted with styrene (**6a**) accompanied by decarboxylation¹⁶ 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.

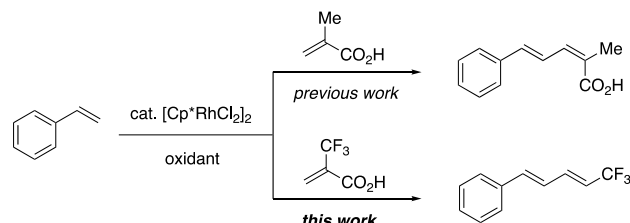
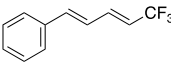
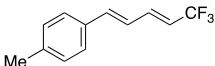
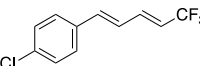
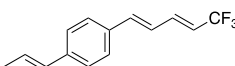
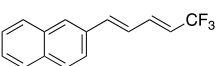
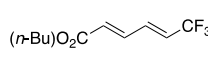
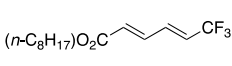
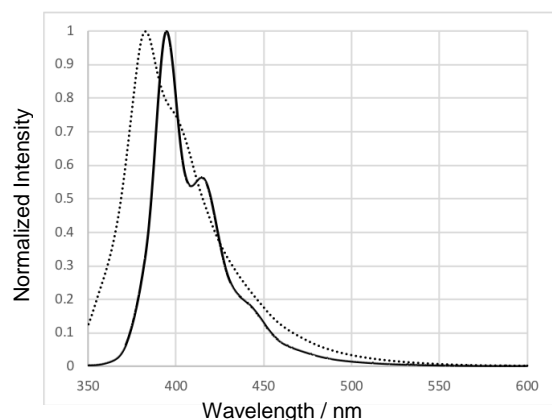
**Scheme 4.**

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

		$\text{R-CH=CH}_2 + \text{CF}_3\text{C(=O)CH=CH}_2 \xrightarrow[\text{NMP}]{[\text{Cp}^*\text{RhCl}_2]_2, \text{AgOAc}}$			
				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*RhCl₂]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*RhCl₂]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.

References and Notes

- For selected reviews, see: a) J. Wang, M. Sánchez-Roselló, J. L. Aceña, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok, H. Liu, *Chem. Rev.* **2014**, *114*, 2432-2506. b) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320-330. c) R. Berger, G. Resnati, P. Metrangola, E. Weber, J. Hulliger, *Chem. Soc. Rev.* **2011**, *40*, 3496-3508. d) D. Anton, *Adv. Mater.* **1998**, *10*, 1197-1205.
- For representative reviews, see: a) X. Liu, C. Xu, M. Wang, Q. Liu, *Chem. Rev.* **2015**, *115*, 683-730. b) T. Liang, C. N. Neumann, T. Ritter, *Angew. Chem., Int. Ed.* **2013**, *52*, 8214-8264. c) K. L. Kirk, *Org. Process Res. Dev.* **2008**, *12*, 305-321.
- For representative reviews, see: a) W. K. Hagmann, *J. Med. Chem.* **2008**, *51*, 4359-4369. b) K. Müller, C. Faeh, F. Diederich, *Science* **2007**, *317*, 1881-1886.
- For example, see: a) C. Almansa, L. A. Gómez, F. L. Cavalcanti, A. F. de Arriba, R. Rodríguez, E. Carceller, J. García-Rafanell, J. Forn, *J. Med. Chem.* **1996**, *39*, 2197-2206. b) S. Watanabe, *Jpn. Kokai Tokkyo Koho* (1992), JP 04063598. c) R. H. Gordonsmith, M. J. Raxworthy, P. A. Gulliver, *Biochem. Pharmacol.* **1982**, *31*, 433-437. d) M. Hu, C. Ni, J. Hu, *J. Am. Chem. Soc.* **2012**, *134*, 15257-15260.
- F. Gelat, A. Patra, X. Pannecoucke, A. T. Biju, T. Poisson, T. Besset, *Org. Lett.* **2018**, *20*, 3897-3901.
- M. Schlosser, *Angew. Chem., Int. Ed.* **2006**, *45*, 5432-5446.
- For reviews, see: a) M. Miura, T. Satoh, K. Hirano, *Bull. Chem. Soc. Jpn.* **2014**, *87*, 751-764. b) T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 11212-11222.
- Prakash, Olah, and co-workers reported an example for the β -arylation of **2**. However, their acid-promoted Friedel-Crafts procedure is applicable only to electron-rich arenes and tends to form mixtures of regioisomers: G. K. S. Prakash, F. Paknia, H. Vaghoo, G. Rasul, T. Mathew, G. A. Olah, *J. Org. Chem.* **2010**, *75*, 2219-2226.
- For recent examples, see: a) Y. Ni, K. Song, K. Shen, Z. Yang, R. Liu, S. Lin, Q. Pan, *Tetrahedron Lett.* **2018**, *59*, 1192-1195. b) R. Liu, Z. Yang, Y. Ni, K. Song, K. Shen, S. Lin, Q. J. Pan, *J. Org. Chem.* **2017**, *82*, 8023-8030. c) L. Zhang, X. Xie, L. Fu, Z. Zhang, *J. Org. Chem.* **2013**, *78*, 3434-3437. d) N. R. Vautravers, B. Breit, *Synlett* **2011**, 2517-2520. e) G. Zou, J. Guo, Z. Wang, W. Huang, J. Tang, *Dalton Trans.* **2007**, 3055-3064. See also reviews: f) T. Miura, M. Murakami, *Chem. Commun.* **2007**, 217-224. g) T. Hayashi, K. Yamasaki, *Chem. Rev.* **2003**, *103*, 2829-2844. h) K. Fagnou, M. Lautens, *Chem. Rev.* **2003**, *103*, 169-196.
- For selected recent reviews for C-H functionalization, see: a) C. Sambigao, D. David Schöbauer, R. Blicke, T. Dao-Huy, G. Pototschnig, P. Schaaf, T. Wiesinger, M. F. Zia, J. Wencel-Delord, T. Besset, B. U. W. Maes, M. A. Schnürch, *Chem. Soc. Rev.* **2018**, *47*, 6603-6743. b) Z. Chen, B. Wang, J. Zhang, W. Yu, Z. Liu, Y. Zhang, *Org. Chem. Front.* **2015**, *2*, 1107-1295. c) G. Song, X. Li, *Acc. Chem. Res.* **2015**, *48*, 1007-1020. d) S. De Sarkar, W. Liu, S. I. Kozhushkov, L. Ackermann, *Adv. Synth. Catal.* **2014**, *356*, 1461-1479. e) J. Wencel-Delord, F. Glorius, *Nat. Chem.* **2013**, *5*, 369-375. f) D. A. Colby, A. S. Tsai, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2012**, *45*, 814-825. g) K. M. Engle, T.-S. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res.* **2012**, *45*, 788-802. h) S. H. Cho, J. Y.

- Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068-5083. i) D. Lapointe, K. Fagnou, *Chem. Lett.* **2010**, *39*, 1118-1126.
- 12 For representative reviews, see: a) Y. Wei, P. Hu, M. Zhang, W. Su, *Chem. Rev.* **2017**, *117*, 8864-8907. b) M. Font, J. M. Quibell, G. J. P. Perry, I. Larrosa, *Chem. Commun.* **2017**, *53*, 5584-5597. c) M. P. Drapeau, L. J. Goossen, *Chem. Eur. J.* **2016**, *23*, 18654-18677. d) T. Satoh, M. Miura, *Synthesis* **2010**, 3395-3409.
- 13 S. Mochida, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2011**, *76*, 3024-3033.
- 14 In most cases, small amounts (~10%) of biphenyl were also formed as a by-product. One of possible roles of Ag₂O seems to be as a reoxidant for a Rh^I species generated during the dimerization of **1a**.
- 15 Under rhodium(I) catalysis, there are several precedents involving an arylation/ β -fluoride elimination sequence: a) T. Miura, Y. Ito, M. Murakami, *Chem. Lett.* **2008**, *37*, 1006-1007. b) Y. Huang, T. Hayashi, *J. Am. Chem. Soc.* **2016**, *138*, 12340-12343. c) Y. J. Jang, D. Rose, B. Mirabi, M. Lautens, *Angew. Chem., Int. Ed.* **2018**, *57*, 16147-16151.
- 16 However, the detailed mechanism of the decarboxylation step is not clear at the present stage.
- 17 For example, see: a) F. B. Sayyed, C. H. Suresh, *J. Phys. Chem A.* **2011**, *115*, 5660-5664. b) F. B. Sayyed, C. H. Suresh, S. R. Gadre, *J. Phys. Chem. A* **2010**, *114*, 12330-12333. c) J. Ignatowska, W. Dmowski, *J. Fluorine. Chem.* **2006**, *127*, 720-729.

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