Received: April 7, 2015 | Accepted: April 23, 2015 | Web Released: May 1, 2015 CL-150322

Copper-mediated One-pot Synthesis of Trifluorostyrene Derivatives from Tetrafluoroethylene and Arylboronate

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We developed the copper-mediated synthesis of trifluorostyrene derivatives. β-Fluorine elimination of a 2-aryl-1,1,2,2-tetrafluoroethylcopper complex, generated in situ from arylboronate, copper *tert*-butoxide, and 1,10-phenanthroline with tetrafluoroethylene (TFE) via carbocupration, was promoted by the addition of a Lewis acid. The present reaction system was applied to the one-pot synthesis of various trifluorostyrene derivatives, through the transmetalation–carbocupration–β-fluorine elimination sequence.

Trifluorovinyl compounds, including trifluorostyrene and its derivatives, could be the favored candidates for a potential monomer for fluorine-containing polymers.[1] To access the trifluorostyrene derivatives, several methods have been reported.[2–8] For example, the reaction of tetrafluoroethylene (TFE) and strong nucleophilic reagents, such as organolithium[3] or organomagnesium compounds,[4] yields the trifluorostyrene derivatives through the addition of the nucleophile to TFE and β-fluorine elimination. The palladium-catalyzed cross-coupling reactions of trifluorovinylzinc, stannane, and boronate compounds with aryl halides have been demonstrated as more direct approaches.[2d,5] Alternatively, a catalytic coupling reaction of aryl nucleophiles with trifluorovinyl halides is also an attractive approach for obtaining trifluorostyrene derivatives.[6,7] The cross-coupling reaction of chloro- or bromotrifluoroethylene with arylboronic acids was reported for obtaining trifluorostyrene derivatives.[6] On the other hand, our group has focused on the catalytic coupling reaction using TFE as a starting material via C–F bond activation.[7] We developed the first palladium-catalyzed arylation of TFE with diarylzinc compounds,[7a,8] arylboronates,[7b] or organosilicon reagents[7c] to give trifluorostyrene derivatives. Additionally, selective monosubstitutions of TFE with diethylzinc or organomagnesium compounds in the presence of a lithium salt have been reported.[8] TFE is one of the most important materials for the production of fluorine-containing polymers such as PTFE and is an economical and environmentally benign feed stock with near-zero global warming potential (GWP) for the fluorine industry.[9] Therefore, the development of transformations of TFE into other valuable organofluorine compounds could increase the potential of TFE as a useful starting material. Very recently, our group demonstrated the synthesis of 2-aryl-1,1,2,2-tetrafluoroethylcopper complexes through the carbocupration[10] of TFE with an arylcopper, prepared from arylboronate, copper *tert*-butoxide, and 1,10-phenanthroline (phen) as a key step.[11] In this literature, we also described that the reaction of phenylmagnesium bromide instead of phenylboronate produced trifluorostyrene. Magnesium salts generated in situ might serve as a Lewis acid and promote the β-fluorine elimination of 2-aryl-1,1,2,2-tetrafluoroethylcopper. To access the trifluorostyrene derivatives bearing various functional groups, however, the use of strong nucleophiles such as organomagnesium compounds should be avoided. In the course of our study, we found that the isolated 2-phenyl-1,1,2,2-tetrafluoroethylcopper complex was converted into trifluorostyrene in the presence of MgBr$_2$.[11] We herein describe the development of the one-pot copper-mediated synthesis of trifluorostyrene derivatives through carbocupration and β-fluorine elimination process using the less expensive copper salt (Figure 1). The present reaction system could be an alternative route toward trifluorostyrene derivatives without palladium catalyst.

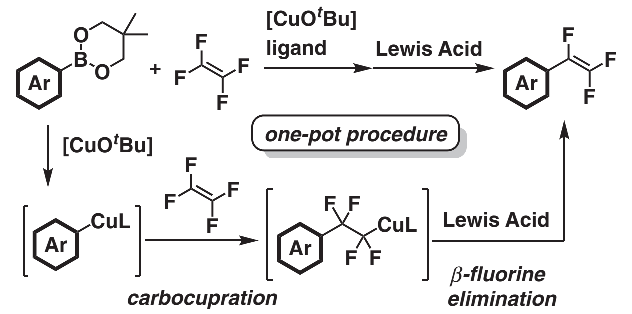


Figure 1. One-pot copper-mediated synthesis of trifluorostyrene derivatives through the transmetalation–carbocupration–β-fluorine elimination process.

The present study was commenced with the examination of the one-pot synthesis of trifluorostyrene from arylboronate and TFE with a copper salt.[12] The mixture of 2-naphthylboronate (**1a**), copper *tert*-butoxide, and phen in THF and THF-d_8 was exposed to TFE (3.5 atm) and stored at 40 °C for 24 h, followed by the addition of LiI. After the mixture was stored at room temperature for 1 h, 2-trifluorovinylnaphthalene (**2a**) was observed on ^{19}F NMR in 57% yield based on the amount of copper salt (Figure 2). Although the desired product was obtained in moderate yield compared with the reaction using isolated 2-phenyl-1,1,2,2-tetrafluoroethylcopper complex and MgBr$_2$ (75%),[11] the one-pot procedure was confirmed to undergo the transmetalation–carbocupration–β-fluorine elimination process to give the corresponding trifluorostyrene derivative. When the reaction was carried out with bathophenanthroline (bathophen) instead of phen, the yield was slightly increased to 67%. The use of 3,4,7,8-tetramethyl-1,10-phenanthroline (Me$_4$-phen) or 2,2′-bipyridine (bpy) as ligands was ineffective and gave no desired product or dropped the yield to 16%, respectively. Although various ligands including phosphine or NHC ligands and other solvents were screened, the yield was not improved (Supporting Information, Tables S1 and S2).

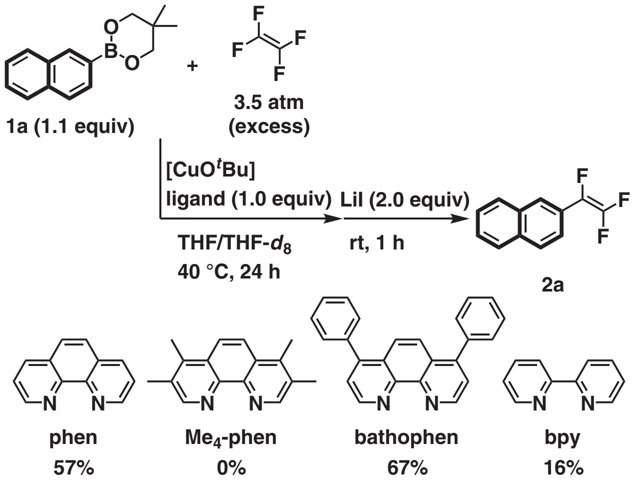
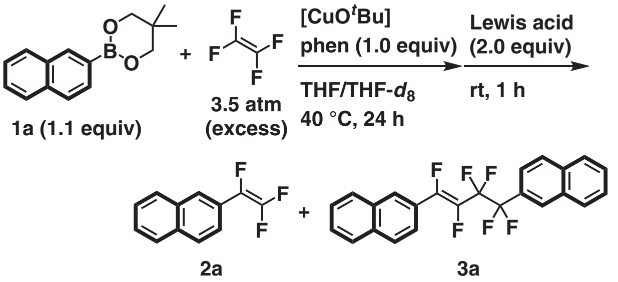


Figure 2. Screening of ligands. General conditions: [CuO^{t}Bu] (0.02 mmol), ligand (0.02 mmol), **1a** (0.022 mmol), $PhCF_3$ (0.02 mmol, as a standard for ^{19}F NMR) in THF/THF-d_8 (0.5 mL, v/v′ = 4/1), TFE (3.5 atm, excess) at 40 °C for 24 h, and then stored at rt for 1 h with LiI (0.04 mmol). Each yield was determined by ^{19}F NMR analysis.

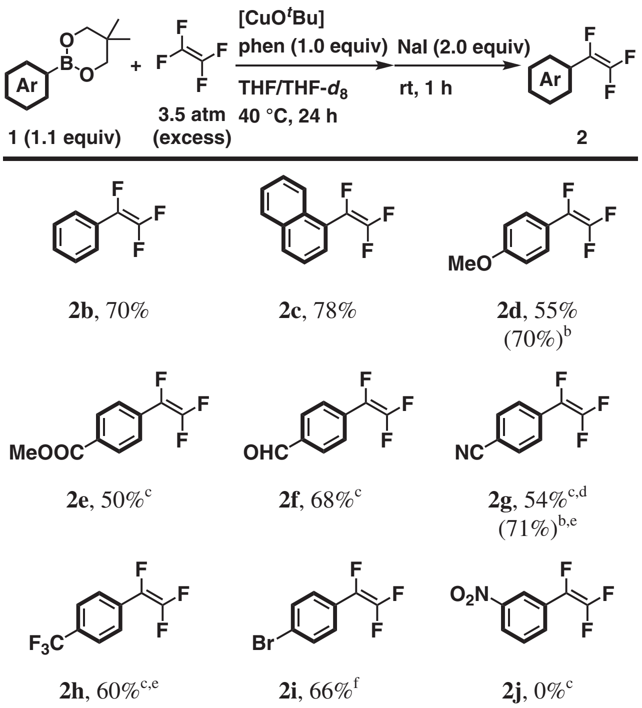
Table 1. Screening of Lewis acids[a]



Run	Lewis acid	Yield/%	
		2a	**3a**
1	$MgBr_2$	61	0
2	NaI	70	0
3	LiI	57	0
4	LiBr	46	5
5	LiCl	25	4
6	LiF	0	0
7	$BF_3\cdot OEt$	0	17

[a]General conditions: [CuO^{t}Bu] (0.02 mmol), phen (0.02 mmol), **1a** (0.022 mmol), $PhCF_3$ (0.02 mmol, as a standard for ^{19}F NMR) in THF/THF-d_8 (0.5 mL, v/v′ = 4/1), TFE (3.5 atm, excess) at 40 °C for 24 h, and then stored at rt for 1 h with Lewis acid (0.04 mmol). Each yield was determined by ^{19}F NMR analysis.

Table 2. Substrate scope[a]



2b, 70% | **2c**, 78% | **2d**, 55% (70%)[b]

2e, 50%[c] | **2f**, 68%[c] | **2g**, 54%[c,d] (71%)[b,e]

2h, 60%[c,e] | **2i**, 66%[f] | **2j**, 0%[c]

[a]General conditions: [CuO^{t}Bu] (0.02 mmol), phen (0.02 mmol), **1** (0.022 mmol), $PhCF_3$ (0.02 mmol, as a standard for ^{19}F NMR) in THF/THF-d_8 (0.5 mL, v/v′ = 4/1), TFE (3.5 atm, excess) at 40 °C for 24 h, and then stored at rt for 1 h with NaI (0.04 mmol). Each yield was determined by ^{19}F NMR analysis. [b]Bathophen was used as a ligand instead of phen. [c]Stored for 48 h before addition of NaI. [d]Heated at 40 °C for 10 h after addition of NaI. [e]Heated at 40 °C for 1 h after addition of NaI. [f]Isolated yield. Reaction conditions: see, Supporting Information.

We next examined the varieties of Lewis acid (Table 1). On using $MgBr_2$, the desired reaction occurred and afforded the desired product **2a** in 61% yield (Run 1). The yield was improved to 70% when NaI was used as the Lewis acid (Run 2). Although LiI caused only β-fluorine elimination and gave **2a** selectively (Run 3), addition of LiBr or LiCl gave a mixture of **2a** contaminated with **3a** (Runs 4 and 5). In these cases, α-fluorine elimination would also occur and the resulting carbene species reacts with 2-trifluoronaphthalene to give **3a**, although the reason is not clear at this time. On the other hand, LiF was ineffective and produced neither **2a** nor **3a** (Run 6). When $BF_3\cdot OEt_2$ was used as the Lewis acid, **2a** was not produced, but only **3a** was obtained in 17% yield (Run 7). Exploration of other Lewis acids did not provide any better results and did not afford any products (Supporting Information, Table S3).

With the optimized reaction conditions in hand, we next surveyed the substrate scope for the copper-mediated one-pot synthesis of trifluorostyrene derivatives using various arylboronates (Table 2). A mixture of arylboronates **1**, copper *tert*-butoxide, and phen in THF and THF-d_8 was exposed to TFE (3.5 atm) and stored at 40 °C for 24 h, followed by the addition of NaI. After the mixture was stored at room temperature for 1 h, the resulting mixture was analyzed by ^{19}F NMR. Starting from 5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane (**1b**) as a boronate, trifluorostyrene (**2b**) was observed on ^{19}F NMR in 70% yield. The present reaction system tolerated electronically and sterically diverse substituents. The reaction using 1-naphthylboronate **1c** proceeded well to yield the corresponding compound **2c** in high yield. Although 4-methoxyphenylboronate **1d** produced **2d** moderately under the standard conditions, the yield was improved to 70% by using bathophen in place of phen. The reaction of arylboronates bearing ester (**1e**) or aldehyde groups (**1f**) also proceeded to give the corresponding compounds **2e** and **f** without any problems. When 4-cyanophenylboronate **1g** was employed, heating at 40 °C and a longer reaction time were required to promote β-fluorine elimination. In this case, changing the ligand to bathophen was effective in giving the desired product **2g** in 71% yield. Additionally, 4-trifluoromethyltrifluorostyrene (**2h**) was generated in 60% yield under the modified reaction conditions. It is notable that the present reaction system exhibits compatibility for bromide **1i** and 4-bromotrifluorostyrene (**2i**) was isolated in 66% yield. In our previous reaction system catalyzed by palladium,[7] bromide was not suitable as a substrate and could not survive. On the other hand, 3-nitrophenylboronate (**1j**) did not yield the desired product even with the present system.

In conclusion, we have developed the copper-mediated synthesis of trifluorostyrene derivatives from arylboronate and TFE through the transmetalation–carbocupration–β-fluorine elimination process under a one-pot procedure. In this system, the carbocupration of TFE was achieved by using in situ generated aryl copper and the β-fluorine elimination of the resulting 2-aryl-1,1,2,2-tetrafluoroethylcopper complex was promoted by the addition of a Lewis acid. The present reaction system does not require strong nucleophiles like organomagnesium compounds or expensive palladium, and provides relatively mild conditions. The application to other reaction systems, including synthesis of trifluorovinylalkane, alkene, or alkyne, and the development of catalytic variants with copper are under investigation in our group.

This work was partially supported by a Grant-in-Aid for Young Scientist (A) (No. 25708018) and a Grant-in-Aid for Scientific Research on Innovative Areas “Molecular Activation Directed toward Straightforward Synthesis” (No. 23105546) from MEXT and by the ACT-C and A-STEP programs from the JST. M.O. also acknowledges The Noguchi Institute.

Supporting Information is available electronically on J-STAGE.

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