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Doctoral Dissertation

Studies on C–F Bond Transformation of Fluoroalkenes via Fluoroalkylcopper Intermediates

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Preface and Acknowledgement

The study in this thesis has been carried out under the direction of Professor Dr. Sensuke Ogoshi at the Department of Applied Chemistry, Faculty of Engineering, Osaka University from April 2013 to March 2018. The thesis described C–F bond transformation of fluoroalkenes via fluoroalkylcopper intermediates.

I would like to express my deepest appreciation to Professor Dr. Sensuke Ogoshi for a number of suggestions, discussions, and encouragement. I would like to express my gratitude to Professor Dr. Nobuaki Kambe and Professor Dr. Naoto Chatani for their stimulating discussions. I would also like to express my special thanks to Associate Professor Dr. Masato Ohashi, Assistant Professor Dr. Yoichi Hoshimoto, Project Assistant Professor Dr. Kotaro Kikushima, and Project Assistant Professor Dr. Kumar Ravindra (CSIR-Central Drug Research Institute, India) for their continuous guidance, advice and assistance. I would like to express my heartfelt appreciation to Ms. Noriko Fujimoto for her kind support and encouragement.

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Contents

Abbreviations

The following abbreviations are used in the thesis.

anal.	Elemental analysis
atm	atmospheric pressure
aq.	aqueous
Ar	aryl
br	broad
Bu	butyl
cat.	catalyst
cf.	confer
CI	chemical ionization
Cy	cyclohexyl
Cyp	cyclopentyl
°C	degrees Celsius
calcd	calculated
d	doublet
δ	chemical shift of NMR signal in ppm
EI	electron ionization
equiv	equivalent
GC	gas chromatography
h	hour(s)
HPLC	high-performance liquid chromatography
HRMS	high-resolution mass specra
Hz	hertz
i	iso
IPr	1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene
J	coupling constant in NMR
L	ligand
M	metal
m	multiplet
m	meta
Me	methyl
min	minute(s)
mL	milliliter
μL	microliter

MS	mass spectral
n	normal
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
o	ortho
ORTEP	Oak Ridge thermal ellipsoid plot
p	para
Ph	phenyl
Phen	1,10-phenanthroline
pin	pinacolato
Pr	propyl
PR_3	trialkyl- or triaryl-phosphine
q	quartet
rt	room temperature
s	singlet
sec	second
t	triplet
t	tertiary
TFE	tetrafluoroethylene
THF	tetrahydrofuran

Chapter 1

General Introduction

Organofluorine compounds have been widely applied in various research fields because of the unique properties of the fluorine atoms.[1] In particular, fluoroalkenes have attracted considerable interest from material scientists and medicinal chemists. Highly fluorinated alkenes have gained much attention as promising monomers for fluorine-containing polymers (Figure 1.1).[2] For instance, trifluoroalkenes and 1,1-difluoroalkenes could be used for the production of modified polytetrafluoroethylenes and ferroelectric polymers respectively. Furthermore, monofluoroalkene units are regarded as structurally equivalent of amide. Fluoroalkene mimics of bioactive amides have been prepared to improve the pharmaceutical properties such as bioactivity, target specificity, and metabolic stability of the bioactive amides.[3] Nevertheless, only a limited range of fluoroalkenes can be prepared by the conventional approaches (Figure 1.2 left). A definitive approach to the synthesis of fluoroalkenes has been to employ the corresponding synthons, such as fluorohaloalkenes and hydrofluorocarbons.[1] This approach strongly depends on the availability of suitable fluorine containing synthons. Therefore, a novel method that allows for the synthesis of diverse fluoroalkene derivatives is anticipated.

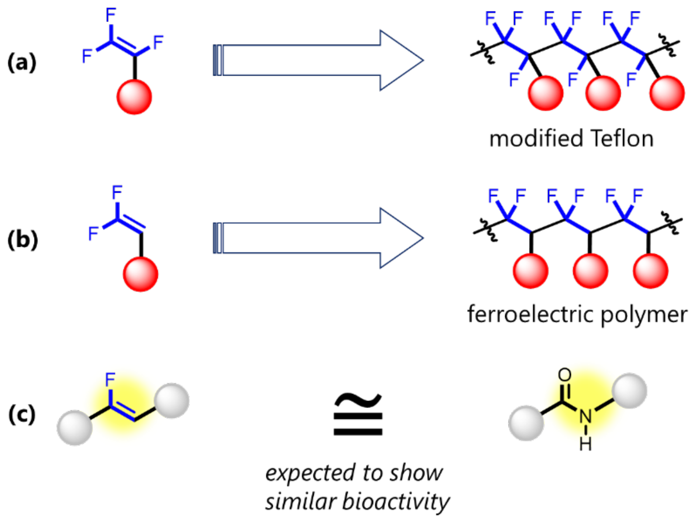


Figure 1.1. Utilities of fluoroalkene moieties

One of the most efficient approaches to synthesize fluoroalkenes would be transformation of polyfluoroalkenes via C–F bond cleavage (Figure 1.2 right). Polyfluoroalkenes such as tetrafluoroethylene (TFE) and its analogues are ideal starting materials for the synthesis of diverse fluoroalkene derivatives as these polyfluoroalkenes represent economical organofluorine feedstocks. However, their use is mostly limited to the production of polymers or refrigerants for air conditioning.

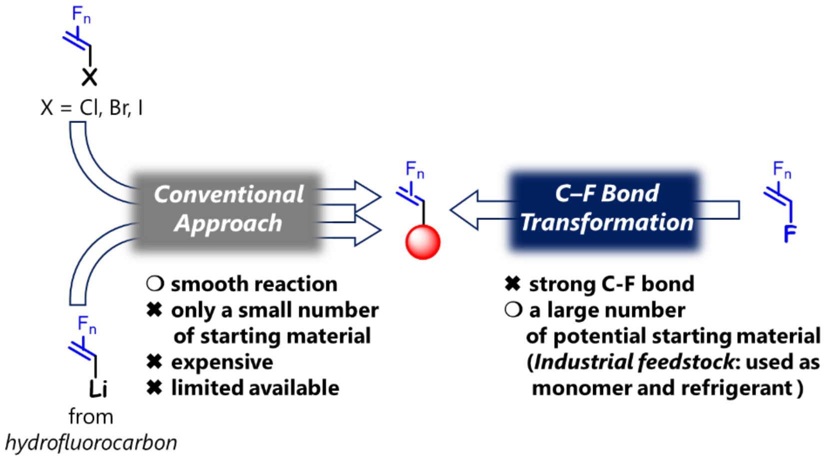


Figure 1.2. Approach to organofluorine compounds

In most cases, C–F bond cleavage was accomplished through oxidative addition by using low-valent transition metal complexes (Figure 1.3).[4] However, a harsh condition is typically required to facilitate oxidative addition of a C–F bond due to its high bond energy. On the other hand, C–F bond cleavage by β-fluorine elimination proceeds under much milder conditions.[5]

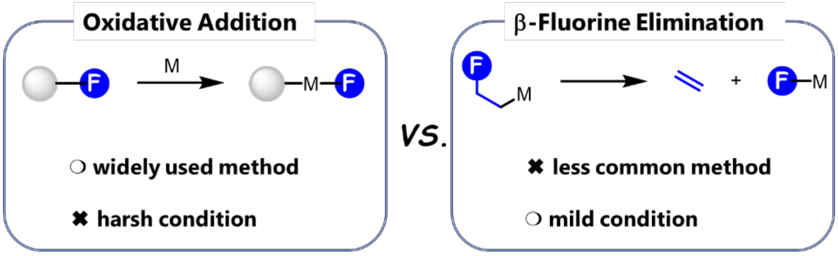
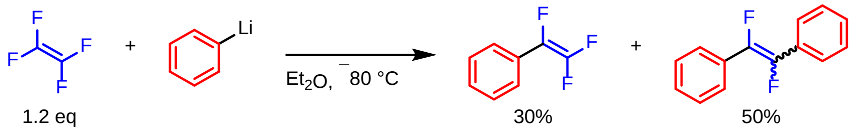
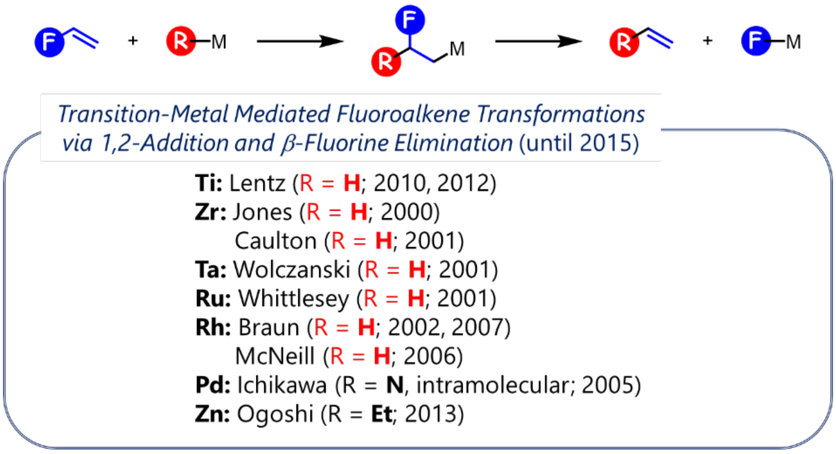


Figure 1.3. C–F bond cleavage on transition metal

It has been known that the combination of 1,2-addition of organometallic species and β-fluorine elimination enables C–F bond transformation of ployfluoroalkenes. For pioneering works, strong nucleophiles such as organolithium or organomagnesium reagents have been used, largely limiting the scope of the substrate.[6] Dixon reported this type of reaction employing the combination of TFE and phenyllithium affording trifluorostyrene (Scheme 1.1).[6a] So far, a number of transition-metal (Ti, Zr, Ta, Ru, Rh, Pd, and Zn) mediated transformations of fluoroalkenes via 1,2-addition and β-fluorine elimination have been developed (Figure 1.4).[7,8,9] However, most of these transformation reactions have been limited to hydrodefluorination reaction.



Scheme 1.1. Pioneering work: reaction of TFE with phenyllithium



Transition-Metal Mediated Fluoroalkene Transformations via 1,2-Addition and β-Fluorine Elimination (until 2015)

Ti: Lentz (R = **H**; 2010, 2012)
Zr: Jones (R = **H**; 2000)
Caulton (R = **H**; 2001)
Ta: Wolczanski (R = **H**; 2001)
Ru: Whittlesey (R = **H**; 2001)
Rh: Braun (R = **H**; 2002, 2007)
McNeill (R = **H**; 2006)
Pd: Ichikawa (R = **N**, intramolecular; 2005)
Zn: Ogoshi (R = **Et**; 2013)

Figure 1.4. 1,2-addition and β-fluorine elimination

In contrast to these transition metals, a variety of organocopper(I) complexes are easily prepared from organoboron compounds (Figure 1.5).[10] Thus, 1,2-addition of organocopper(I) to polyfluoroalkenes would afford a new class of fluoroalkylcopper(I) intermediate that allows us to develop a novel synthetic route to organofluorine compounds that are difficult to access by conventional methods. Furthermore, polyfluoroalkenes should be able to undergo 1,2-addition of organocopper(I) smoothly because their electrophilic nature makes the backdonation from Cu(I) center to them stronger than non-fluorinated alkenes.

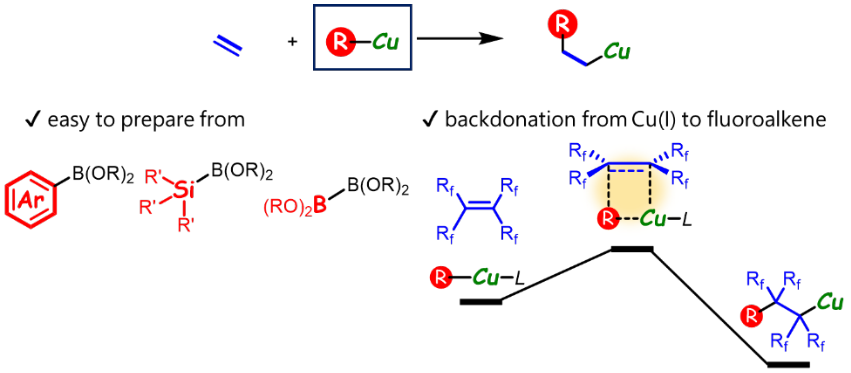
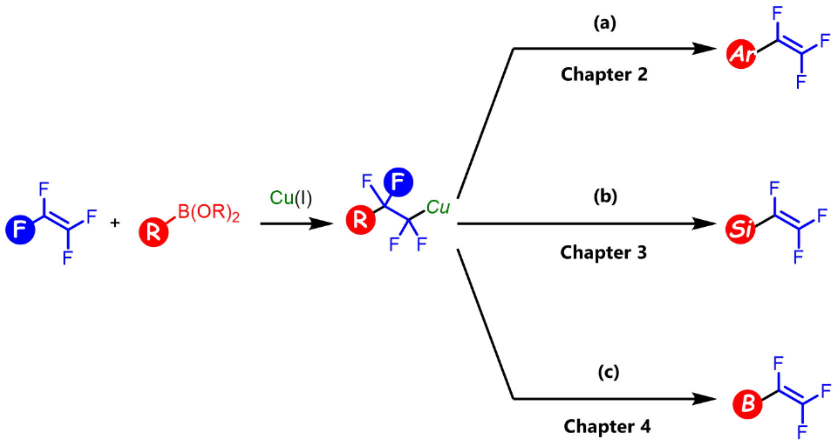


Figure 1.5. Organocopper(I) complexes

In this thesis, the purpose of this study is the development of C–F bond transformation reactions of ployfluoroalkenes via fluoroalkylcopper key intermediates. This thesis consists of the general introduction and the following three chapters (Scheme 1.2). In chapter 2, one-pot synthesis of trifluorostyrene derivatives from TFE and arylboronate via the carbocupration is described (Scheme 1.2 (a)). Chapter 3 deals with a copper-catalyzed defluorosilylation reaction of TFE and other polyfluoroalkenes (Scheme 1.2 (b)). In chapter 4, the development of a copper-catalyzed regioselective defluoroborylation of polyfluoroalkenes is discussed (Scheme 1.2 (c)). Finally, this thesis is summarized in conclusion.



Scheme 1.2. This thesis: a) one-pot synthesis of trifluorostyrene derivatives from TFE and arylboronate via the carbocupration, b) a copper-catalyzed defluorosilylation reaction of TFE and other polyfluoroalkenes, c) a copper-catalyzed regioselective defluoroborylation of polyfluoroalkenes

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Chapter 2

One-Pot Synthesis of Trifluorostyrene Derivatives from Tetrafluoroethlene and Arylboronate via Carbocupration

2.1 Introduction

Trifluorostyrene derivatives are the favored candidate for a potential monomer of functional polymers such as ion exchange membranes for fuel cell separators (Figure 2.1).[1]

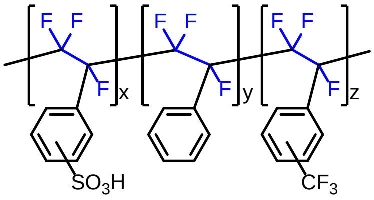
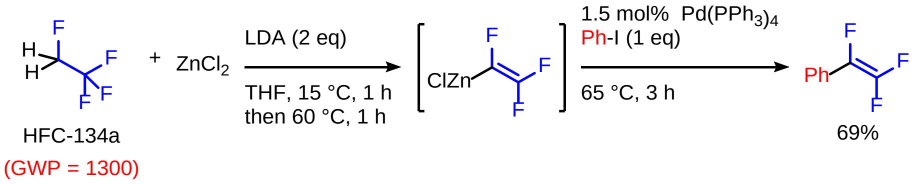


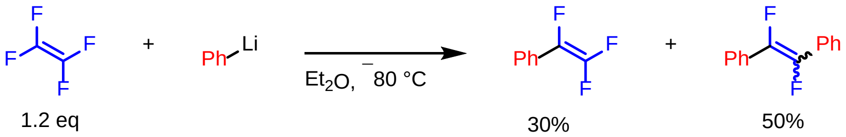
Figure 2.1. BAM® membrane for fuel cell

To synthesize trifluorostyrene derivatives, the Pd(0)-catalyzed coupling reaction of iodoarenes with trifluorovinylzinc chloride which is prepared from 1,1,1,2-tetrafluoroethane (HFC-134a) had been the most straightforward method (Scheme 2.1).[2] However, HFC-134a has been no longer available since 2015 due to the high global warming potential (GWP). Thus, an alternative synthetic approach to trifluorostyrene derivatives have been highly required.



Scheme 2.1. Synthesis of trifluorostyrene from HFC-134a

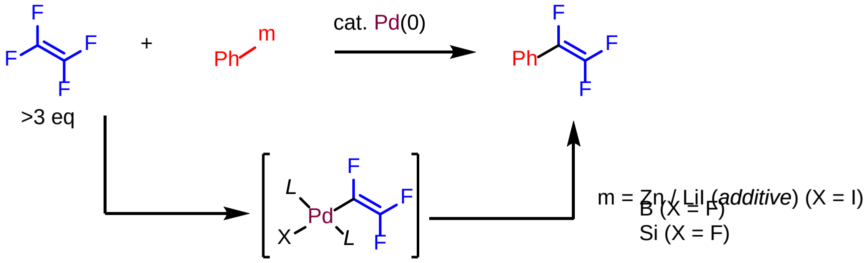
TFE is one of the most important materials for the production of fluorine-containing polymers such as PTFE and an economical and environmentally benign fluorine industry feed stock with near-zero GWP.[3] Therefore, TFE is an ideal starting material for the production of trifluorostyrene derivatives. It has been known that the reaction of TFE with strong nucleophilic reagents, such as organolitium[4] or organomagnesium compounds,[5] affords trifluorostyrene derivatives through 1,2-addition and β-fluorine elimination pathway (Scheme 2.2). However, these reactions are suffered from low functional group tolerance and the undesired formation of disubstituted product, 1,2-diaryl-1,2-difluoroethylene, resulted from the further reaction of trifluorostyrene with strong nucleophilic reagents.



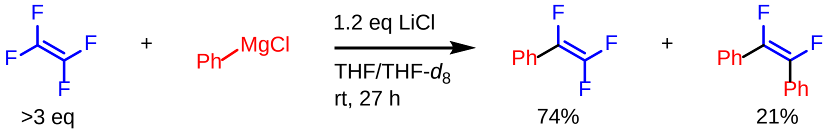
Scheme 2.2. Synthesis of trifluorostyrene from TFE and phenyllithium reagent

Our group has also made an effort to develop an alternative route to trifluorostyrene derivatives from TFE. For instance, palladium-catalyzed coupling reactions of TFE with diarylzinc compounds,[6a] organoboron reagent,[6b] or organosilicon reagent,[6c] furnished the trifluorostyrene derivatives (Scheme 2.3 (a)). Additionally, selective monosubstitutions of TFE with diethylzinc or organomagnesium compound in the presence of lithium salt have been reported (b).[7] Furthermore, our group demonstrated the synthesis of 2-aryl-1,1,2,2-tetrafluoroethylcopper complexes through the carbocupration of TFE with an arylcopper, which was prepared from arylboronate, CuO^{t}Bu, and 1,10-phenanthroline (Phen) as a key step (c).[8] In this literature, it was also disclosed that a treatment of these fluoroalkylcopper species with $MgBr_2$ prompted the β-fluorine elimination to afford the corresponding trifluorostyrene derivatives.

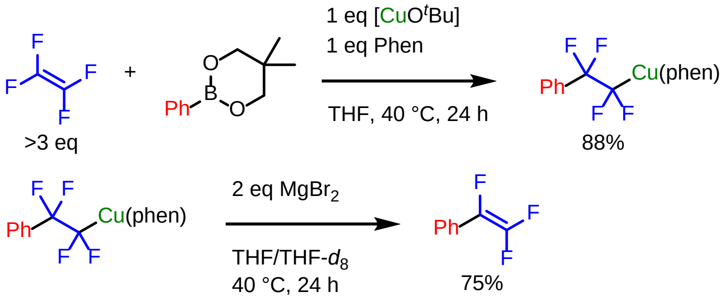
(a) Pd(0)-catalyzed coupling reaction of TFE with organometallic reagent



(b) LiCl promoted reaction of TFE with organomagnesium reagents

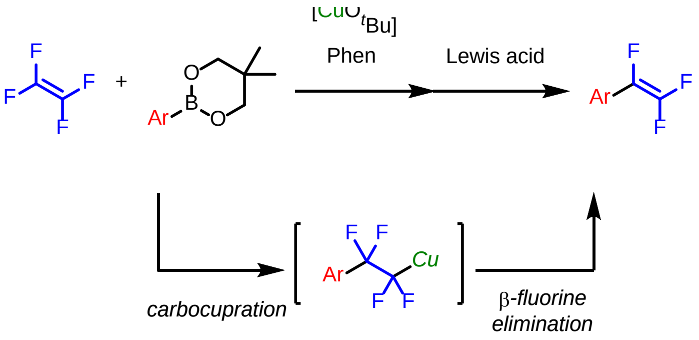


(c) Synthesis and reactivity of 2-phenyl-1,1,2,2-tetrafluoroethylcopper complex



Scheme 2.3. Our group approaches

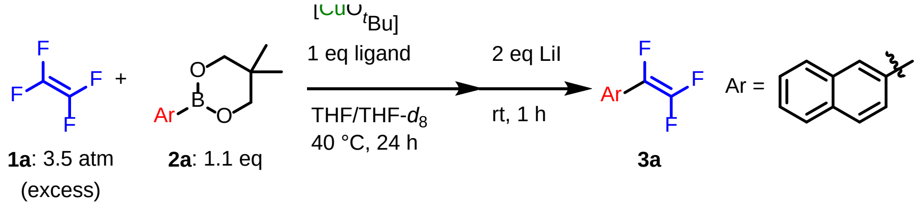
Described in this chapter is one-pot copper-mediated synthesis of trifluorostyrene derivatives through carbocupration and β-fluorine elimination process (Scheme 2.4). The present system could be the alternative route the trifluorostyrene derivatives without palladium catalyst.



Scheme 2.4. One-pot synthesis of trifluorostyrene derivatives by carbocupration of TFE

2.2 Optimization of reaction condition (ligand)

The mixture of 2-naphthylboronate (**2a**), CuO^{t}Bu, and Phen in THF/THF-d_8 was exposed to TFE (**1a**, 3.5 atm; excess amount) and stored at 40 °C for 24 h, followed by addition of LiI. After the mixture was stored at room temperature for 1 h, The formation of 2-trifluorovinylnaphthalene (**3a**) was confirmed by ^{19}F NMR in 57% yield based on the amount of CuO^{t}Bu (Table 2.1, run 1). 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%),[8] 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% (run 2). The use of 3,4,7,8-tetramethyl-1,10-phenanthroline or 2,2'-bipyridine as ligands was ineffective and gave no desired product or dropped the yield to 16%, respectively (runs 3 and 4). Although various ligands including phosphine ligands or NHC ligand were screened, the yield was not improved (runs 5-14).



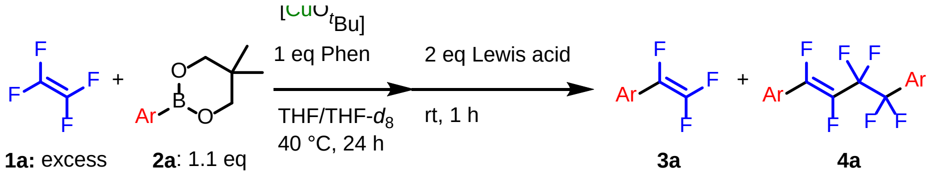
run	ligand	yield[a]	run	ligand	yield[a]
1	Phen	57%	8	DPPM	0%
2	Bathophen	67%	9	DPPB	23%
3	3,4,7,8-Me_4Phen	0%	10	DCPB	7%
4	2,2'-bipyridine	16%	11	DPPF	44%
5	PCy_3(2 eq)	0%	12	BINAP	9%
6	PPh_3 (2 eq)	0%	13	Xantphos	17%
7	PPh_3 (3 eq)	0%	14	IPr	0%

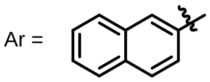
[a] ^{19}F NMR yield based on [CuO^{t}Bu](0.02 mmol)

Table 2.1. Ligand screening

2.3 Effect of Lewis acid on β-fluorine elimination

Next, the varieties of Lewis acid were examined (Table 2.2). Using $MgBr_2$ underwent the desired reaction and afforded the desired product **3a** in 61% yield (run 1). The reaction yield was improved to 70% when NaI was used (run 2). Although the use of LiI caused β-fluorine elimination and yielded **3a** selectively (run 3), addition of LiBr or LiCl gave the mixture of **3a** contaminated with 2,2'-(perfluorobutene-1,4-diyl)dinaphthalene (**4a**) (runs 4 and 5). On the other hand, LiF was ineffective to produce neither **3a** nor 4**a** (run 6). When BF_3•OEt_2 was used as a Lewis acid, 3**a** was not produced, but **4a** was obtained in 34% yield (run 7).





run	Lewis acid	yield^a	
1	$MgBr_2$	61%	0%
2	NaI	70%	0%
3	LiI	57%	0%
4	LiBr	46%	5%
5	LiCl	25%	8%
6	LiF	0%	0%
7	$BF_3 \cdot OEt_2$	0%	34%

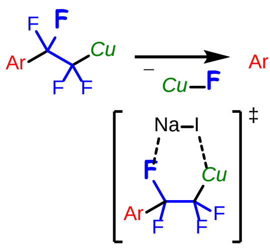
[a] ^{19}F NMR yield based on [CuO^{t}Bu](0.02 mmol)

Table 2.2. Effect of Lewis acid on fluorine elimination

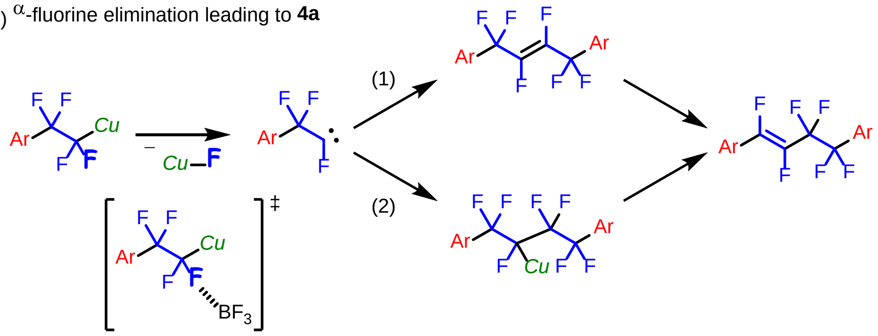
2.3 A possible reaction mechanism

In the case of the reaction of the fluoroalkylcopper complex with $MgBr_2$, LiI or NaI, **3a** is given via six-menbered transition state which is proposed by Ishihara (Scheme 2.5 a).[9] On the other hand, in the case of BF_3•OEt_2, α-fluorine elimination would occur. There are at least two possible reaction pathways leading to **4a**; 1) dimerization of the resulting fluorocarbene species followed by fluorine migration to give **4a**, or 2) insertion of the carbene into a Cu–C bond of the fluoroalkylcopper followed by β-fluorine elimination to give **4a**.[10] However, the detail is not clear at this time.

(a) β-fluorine elimination leading to **3a**



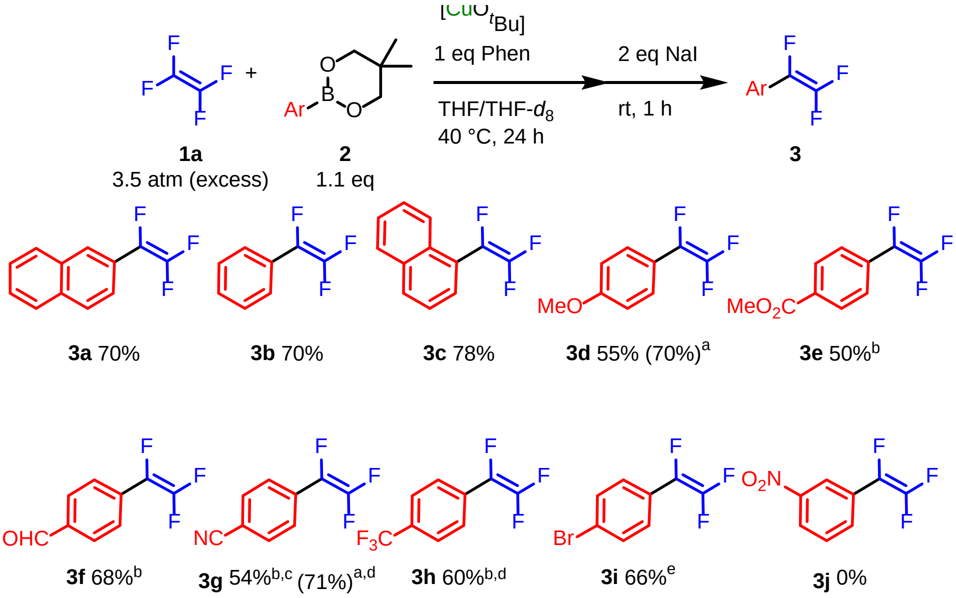
(b) α-fluorine elimination leading to **4a**



Scheme 2.5. A possible reaction pathway

2.4 Substrate scope

With the optimized reaction conditions in hand, the substrate scope for the copper-mediated one-pot synthesis of trifluorostyrene derivatives was investigated (Table 2). When 5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane (**2b**) was used, the generation of trifluorostyrene (**3b**) was observed on ^{19}F NMR in 70% yield. The present reaction system tolerated electronically and sterically diverse substituents. The reaction using 1-naphthylboronate (**2c**) proceeded to give the corresponding compound (**3c**) in 78% yield. In the case of 4-methoxyphenylboronate (**2d**), the reaction gave **3d** in moderate yield under standard conditions. The yield was improved to 70% by using bathophenanthroline instead of Phen. The reaction of arylboronates bearing an ester (**2e**) or a formyl group (**2f**) also proceeded to yield the corresponding compounds (**3e** and **3f**). When 4-cyanophenylboronate (**2g**) was employed, heating at 40 °C and a longer reaction time were required to undergo β-fluorine elimination. In this case, the use of bathophenanthroline was effective to afford the desired product (**3g**) in 71% yield. Furthermore, 4-trifluoromethyltrifluorostyrene (3**h**) was gived in 60% yield under the modified reaction conditions. It should be mentioned that the present system exhibits compatibility for 4-bromophenyl boronate (**2i**) and 4-bromotrifluorostyrene (**3i**) was isolated in 66% yield. In our previous system, Pd(0)-catalyzed coupling reaction of TFE with organometallic reagents,[6] 4-bromophenyl boronate (**2i**) was not suitable as a substrate because undesired oxidative addition of C–Br bond occurred predominantly. On the other hands, 3-nitropehnylboronate (2**j**) did not provide the desired product even with the present system. In this case, the carbocupration did not proceed at all.



Scheme 2.6. Substrate scope; [a] Bathophenanthroline was used as a ligand instead of 1,10-phenanthroline. [b] For 48 h before addition of NaI. [c] Heated at 40 °C for 10 h after addition of NaI. [d] Heated at 40 °C for 1 h after addition of NaI. [e] Isolated yield.

2.5 Conclusion

In chapter 2, the copper-mediated one-pot synthesis of trifluorostyene derivatives from arylboronate and TFE via carbocupration is described. In this system, carbocupration of TFE is achieved by employing aryl copper in situ generated and the β-fluorine elimination of the resulting fluoroalkylcopper complex was promoted by the addition of proper Lewis acid. The present reaction system does not require strong nucleophiles such as organomagnesium compound or expensive palladium.

2.6 References and notes

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2.7 Experimental section

General remarks compatible to all the experimental part in this thesis

All manipulations were conducted under a nitrogen atmosphere using standard Schlenk or dry box techniques. ^{1}H, ^{13}C, and ^{19}F nuclear magnetic resonance (NMR) spectra were recorded on Bruker Avance III 400 spectrometer. The chemical shifts in ^{1}H and ^{13}C NMR spectra were recorded relative to residual protonated solvent ($CHCl_3$ (δ 7.26 ppm for ^{1}H NMR and δ 77.16 ppm for ^{13}C NMR), C_6D_6 (δ 7.16 ppm for ^{1}H NMR) and THF-d_8 (δ 3.58 ppm for ^{1}H NMR and δ 67.21 ppm for ^{13}C NMR)). The chemical shifts in ^{19}F NMR spectra were recorded relative to α,α,α-trifluorotoluene (δ -65.4 ppm) as an internal standard. Mass spectra were obtained using a Shimadzu GCMS-QP 2010 instrument with an ionization voltage of 70 eV. Analytical gas chromatography was carried out on a Shimadzu GC-2014 gas chromatograph, equipped with a flame ionization detector. High resolution mass spectrometry (HRMS) was performed at Instrumental Analysis Center, Faculty of Engineering, Osaka University.

Material for all the experimental part in this thesis

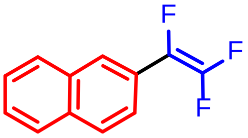
All commercially available reagents were used as received unless otherwise noted. C_6D_6, THF, and THF-d_8 were distilled from sodium benzophenone ketyl. Arylboronates **2** were prepared by esterification of the corresponding arylboronic acids with 2,2-dimethylpropandiol,[S1] CuO^{t}Bu,[S2] (IPr)CuCl,[S3] (IPr)CuO^{t}Bu,[S4] NHC,[S5] (3,3,3-trifluoro-1-propen-2-yl)benzene (**1g**),[S6] 1-(trifluorovinyl)naphthalene,[S7] 2-(trifluorovinyl)naphthalene,[S7] and fluorodimethylphenylsilane[S8] were prepared according to the literatures. Fluoroalkenes (**1a**-**1f** and chlorotrifluoroethylene) were kindly supplied by from Daikin Industries, Ltd.

Caution: Tetrafluoroethylene (TFE) is suspected to be carcinogens. The reaction mixture must be handled in a well-ventilated fume hood

General procedure (for monitoring of the reaction by ^{19}F NMR, Figure 2, Scheme 2.6)

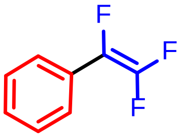
The reactions were conducted with a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7). To a solution of CuO^{t}Bu (2.7 mg, 0.02 mmol) and ligand in THF/THF-d_8 (v/v' = 4/1) (0.5 mL) was added arylboronic acids (**2**, 0.022 mmol, 1.1 eq) and α,α,α-trifluorotoluene (2.4 µL, 0.02 mmol; as an internal standard for ^{19}F NMR). The resultant solution was transferred into the tube, and then TFE (3.5 atm, excess) was pressurized. After the reaction mixture was heated at 40 °C for 24 h, Lewis acid (0.04 mmol, 2 eq) was added. Monitoring the reaction was performed by means of ^{19}F NMR spectroscopy. The yields of **3** were determined by ^{19}F NMR spectroscopy using α,α,α-trifluorotoluene as an internal standard.

2-(1,2,2-trifuluorovinyl)naphthalene (3a)



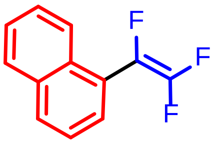
Following a modification of the general procedure, the reaction using 5,5-dimethyl-2- (2-naphthyl)-1,3,2-dioxaborinane (**2a**) was conducted. The formation of **3a** (0.014 mmol, 70%) was confirmed by ^{19}F NMR and GCMS analysis. ^{19}F NMR (376 MHz, THF/THF-d_8, 22 °C, δ/ppm): -178.6 (dd, J_{FF} = 108.8, 32.0 Hz, 1F), -117.0 (dd, J_{FF} = 108.8, 70.6 Hz, 1F), -103.4 (dd, J_{FF} = 70.6, 32.0 Hz, 1F). MS (EI): *m/z* (%): 208 (100) [M]+, 157 (37), 127 (10). Spectral data of **3a** were identical to that previously reported.[S9]

α,β,β-trifluorostyrene (3b)



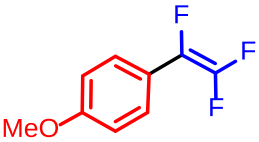
Following a modification of the general procedure, the reaction using 5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane (2**b**) was conducted. The formation of **3b** (0.014 mmol, 70%) was confirmed by ^{19}F NMR and GCMS analysis. ^{19}F NMR (376 MHz, THF/THF-d_8, 22 °C, δ/ppm): -179.2 (dd, J_{FF} =110.3, 32.7 Hz, 1F), -118.5 (dd, J_{FF} = 110.3, 73.5 Hz, 1F), -104.2 (dd, J_{FF} = 73.5, 32.7 Hz, 1F). MS (EI): *m/z* (%): 158 (100) [M]+, 107 (28). Spectral data of **3b** were identical to that previously reported.[S9]

1-(1,2,2-trifuluorovinyl)naphthalene (3c)



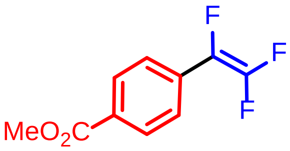
Following a modification of the general procedure, the reaction using 5,5-dimethyl-2- (1-naphthyl)-1,3,2-dioxaborinane (**2c**) was conducted. The formation of **3c** (0.016 mmol, 78%) was confirmed by ^{19}F NMR and GCMS analysis. ^{19}F NMR (376 MHz, THF/THF-d_8, 22 °C, δ/ppm): -162.1 (dd, J_{FF} = 117.7, 29.8 Hz, 1F), -120.7 (dd, J_{FF} = 117.7, 75.2 Hz, 1F), -105.7 (dd, J_{FF} = 75.2, 29.8 Hz, 1F). MS (EI): *m/z* (%): 208 (100) [M]+, 157 (41), 127 (14). Spectral data of **3c** were identical to that previously reported. [S10]

1-methoxy-4-(1,2,2-trifuluorovinyl)benzene (3d)



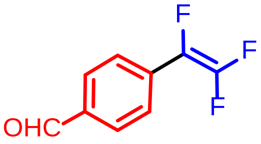
Following a modification of the general procedure (using Bathophen as a ligand), the reaction using 5,5-dimethyl-2- (4-methoxyphenyl)-1,3,2-dioxaborinane (**2d**) was conducted. The formation of **3d** (0.014 mmol, 70%) was confirmed by ^{19}F NMR and GCMS analysis. ^{19}F NMR (376 MHz, THF/THF-d_8, 22 °C, δ/ppm): -177.4 (dd, J_{FF} = 110.0, 31.7 Hz, 1F), -121.1 (dd, J_{FF} = 110.0, 77.7 Hz, 1F), -106.6 (dd, J_{FF} = 77.7, 31.7 Hz, 1F). MS (EI): *m/z* (%): 188 (69) [M]+, 173 (43), 145 (100), 107 (11). Spectral data of **2d** were identical to that previously reported.[S9]

methyl-4-(1,2,2-trifluorovinyl)benzoate (3e)



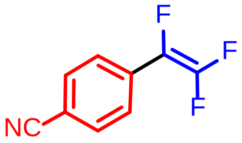
Following a modification of the general procedure, the reaction using methyl 4-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)benzoate (**2e**) was conducted. The formation of **3e** (0.010 mmol, 50%) was confirmed by ^{19}F NMR and GCMS analysis. ^{19}F NMR (376 MHz, THF/THF-d_8, 22 °C, δ/ppm): -180.2 (dd, J_{FF} = 110.0, 31.7 Hz, 1F), -115.0 (dd, J_{FF} = 110.0, 77.7 Hz, 1F), -101.1 (dd, J_{FF} = 77.7, 31.7 Hz, 1F). MS (EI): *m/z* (%): 216 (47) [M]+, 185 (100), 157 (50), 137 (69). Spectral data of **2e** were identical to that previously reported.[S11]

4-(1,2,2-trifluorovinyl)benzaldehyde (3f)



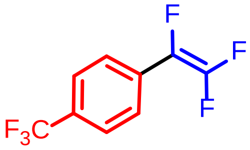
Following a modification of the general procedure, the reaction using 4-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)benzaldehyde (**2f**) was conducted. The formation of **3f** (0.014 mmol, 68%) was confirmed by ^{19}F NMR and GCMS analysis. ^{19}F NMR (376 MHz, THF/THF-d_8, 22 °C, δ/ppm): -180.1 (dd, J_{FF} = 110.0, 31.7 Hz, 1F), -114.3 (dd, J_{FF} = 110.0, 77.7 Hz, 1F), -100.4 (dd, J_{FF} = 77.7, 31.7 Hz, 1F). MS (EI): *m/z* (%):186 (95) [M]+, 185 (80), 157 (69), 137 (100), 105 (12). Spectral data of 3**f** were identical to that previously reported.[S9]

4-(1,2,2-trifluorovinyl)benzonitrile (3g)



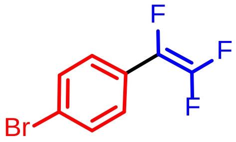
Following a modification of the general procedure (using Bathophen as a ligand, heated at 40 °C for 1 h after addition of NaI), the reaction using 4-(5,5-dimethyl- 1,3,2-dioxaborinan-2-yl)benzonitrile (**2g**) was conducted. The formation of **3g** (0.014 mmol, 71%) was confirmed by ^{19}F NMR and GCMS analysis. ^{19}F NMR (376 MHz, THF/THF-d_8, 22 °C, δ/ppm): -180.7 (dd, J_{FF} = 110.0, 31.7 Hz, 1F), -114.6 (dd, J_{FF} = 110.0, 77.7 Hz, 1F), -99.8 (dd, J_{FF} = 77.7, 31.7 Hz, 1F). MS (EI): *m/z* (%): 183 (100) [M]+, 163 (20), 133 (42), 132 (39). Spectral data of **3g** were identical to that previously reported.[S10]

1-trifluoromethyl-4-(1,2,2-trifuluorovinyl)benzene (3h)



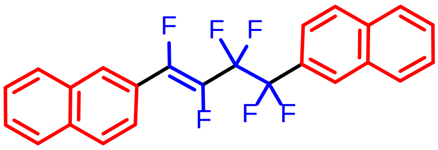
Following a modification of the general procedure (heated at 40 °C for 1 h after addition of NaI), the reaction using 5,5-dimethyl-2- (4-trifluorometylphenyl)-1,3,2-dioxaborinane (**2h**) was conducted. The formation of **3h** (0.012 mmol, 60%) was confirmed by ^{19}F NMR and GCMS analysis. ^{19}F NMR (376 MHz, THF/THF-d_8, 22 °C, δ/ppm): -180.3 (dd, J_{FF} = 109.2, 33.9 Hz, 1F), -117.3 (dd, J_{FF} = 109.2, 64.0 Hz, 1F), -103.1 (dd, J_{FF} = 64.0, 33.9 Hz, 1F), -65.5 (s, 3F). MS (EI): *m/z* (%): 226 (100) [M]+, 202 (20), 176 (26), 157 (30). Spectral data of **3h** were identical to that previously reported.[S9]

1-bromo-4-(1,2,2-trifluorovinyl)benzene (3i)



In an autoclave reactor, CuO^{t}Bu (67.5 mg, 0.50 mmol), 1,10-phenanthlorine (90.0 mg, 0.50 mmol), and 5,5-dimethyl-2- (4-bromophenyl)-1,3,2-dioxaborinane (**2i**) (161 mg, 0.60 mmol) was dissolved in 10.0 mL of THF. TFE (3.5 atm) was pressurized into the reactor. The reaction mixture was heated at 40 °C for 24 h. After the unreacted TFE was purged from the reactor (***caution***: The reaction mixture must be handled in a well-ventilated fume hood.), the reaction mixture was concentrated *in vacuo*. 10.0 mL of pentane was added to the residue, and the resulting suspension was filtered through a short silica column. The title compound (**3i**) was isolated by preparative HPLC ($CHCl_3$) in 66% yield (77.7 mg) as a colorless oil. ^1H NMR (400 MHz, in $CDCl_3$, 22 °C, δ/ppm): 7.33 (d, 2H), 7.56 (d, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, in $CDCl_3$, 22 °C, δ/ppm): 123.0 (m), 126.0 (m), 126.4 (dd, J_{CF} = 22.6, 7.1 Hz), 128.3 (ddd, J_{CF} = 226.2, 44.1, 19.5 Hz), 132.1, 153.7 (ddd, J_{CF} = 291.2, 282.9, 50.2 Hz). ^{19}F NMR (376 MHz, THF/THF-d_8, 22 °C, δ/ppm): -179.6 (dd, J_{FF} = 109.2, 33.9 Hz, 1F), -117.0 (dd, J_{FF} = 109.2, 64.0 Hz, 1F), -102.9 (dd, J_{FF} = 64.0, 33.9 Hz, 1F), -65.5 (s, 3F). HRMS Calcd for $C_8H_4BrF_3$ 235.9448, found *m/z* 235.9451.

(E)-2,2'-(perfluorobut-1-ene-1,4-diyl)dinaphthalene (4a)



^{19}F NMR (376 MHz, in THF-d_8, 22 °C, δ/ppm): –166.8 (dtt, J_{FF} = 130.8, 11.6, 5.4 Hz, 1F), –147.3 (dtt, J_{FF} = 130.8, 27.5, 7.1 Hz, 1F), –119.2 (ddt, J_{FF} = 27.5, 11.6, 3.9 Hz, 2F), –114.6 (m, 2F), HRMS Calcd for $C_{16}H_{11}F_3$ 416.1000 found *m/z* 416.0997.

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Chapter 3

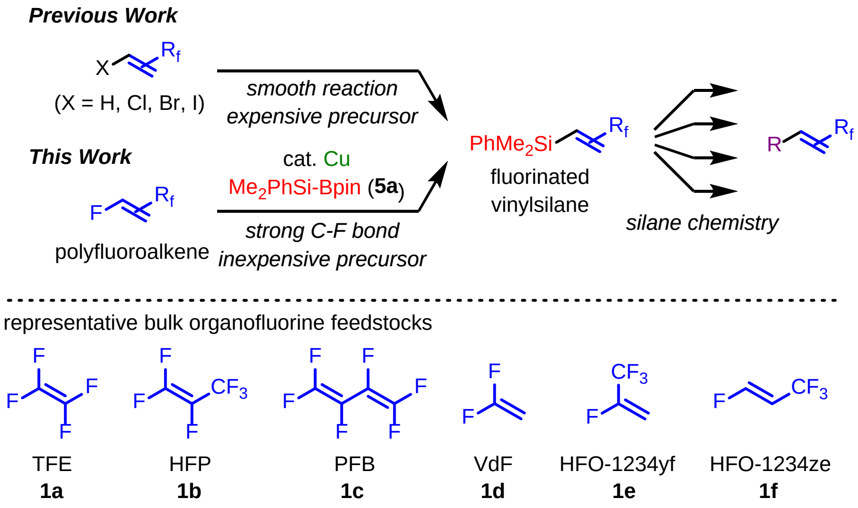
Cu(I)-Catalyzed Defluorosilylation of Polyfluoroalkenes

3.1 Introduction

Organofluorine compounds have attracted much attention on account of their remarkable applications in pharmaceutical and materials sciences.[1] So far, most research has been aimed at the development of methods for the selective introduction of either fluorine atoms or fluorinated building blocks in organic molecules. Practical approaches usually include fluorinated organosilicon reagents such as the Ruppert–Prakash reagent (trifluoromethyltrimethylsilane), which are easy to handle and store, and exhibit high stability and low toxicity.[2] Fluorinated vinylsilanes have shown great promise as a powerful tool for the introduction of fluorinated vinyl moieties in organic molecules, given that vinylsilanes represent versatile building blocks in organic synthesis.[3] However, a straightforward synthetic approach to fluorinated vinylsilanes remains elusive because almost all relevant starting materials are either expensive or not easily available (Scheme 3.1).[4]

Polyfluoroalkenes such as TFE and its analogues (**1a**–**1f**) are ideal starting materials as they represent economical organofluorine feedstocks. Thus, defluorosilylation of polyfluoroalkenes, silylative cleavage of C–F bond in polyfluoroalkenes, would be a powerful tool to access fluorinated vinylsilanes. As described in Chapter 2, a Lewis acid-promoted β-fluorine elimination of 2-aryl-1,1,2,2-tetrafluoroethylcopper, yielding trifluorostyrene derivatives, is disclosed. Thus, the silylcupration of TFE should be achieved. Although silylcuprations across C–C multiple bonds are usually reliable and powerful,[5] silylcuprations of fluorinated alkenes remain unexplored thus far. Furthermore, β-fluorine elimination leading to Cu–F species should enable a catalytic transformation into fluorinated vinylsilanes.

Described in this chapter is a copper-catalyzed transformation of polyfluoroalkenes into vinylsilane derivatives via cleavage of the C–F bond. In this reaction, a fluoroalkylcopper(I) intermediate generated by the silylcupration of TFE was found to undergo β-fluorine elimination to generate a copper(I) fluoride species, which enables the catalytic reaction to proceed.



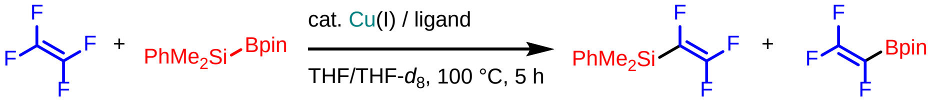
Scheme 3.1. Synthesis of fluorinated vinylsilanes

3.2 Development of the catalytic reaction (Ligand screening)

In the presence of 10 mol% CuO^{t}Bu and 10 mol% 1,1'-bis(diphenylphosphino)ferrocene (dppf), the reaction of Me$_2$PhSi–Bpin (**5a**) with TFE (**1a**) at 100 °C afforded trifluorovinylphenyldimetylsilane (**6a**) in 58% yield under concomitant formation of the undesired 2-trifluorovinyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**7a**) in 30% yield (Table 3.1, run 1). After screening some potential ligands, 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr) was the best ligand for this catalytic system (run 9).

3.3 Optimization of reaction condition (2)

Reduction of the catalyst loading to 5 mol% (IPr)CuO^{t}Bu decreased the rate of the reaction (Table 3.2, run 1). By using F–Bpin generated from H–Bpin and NEt$_3$·3HF[6] as an additive, the yield of **6a** was improved to 79% (run 2). The use of either a larger amount of F–Bpin as an additive was not effective for further improvement of the yield of **6a** (run 3-5). The use of (IPr)CuF instead of (IPr)CuO^{t}Bu resulted in the best yield of **6a**, whereby the addition of F–Bpin is not required (run 6). This may be rationalized by the *in situ* generation of F–Bpin from the reaction of (IPr)CuF with **5a** as the first step of the catalytic reaction. The yield was not improved when other potential additives were employed (run 7-11).

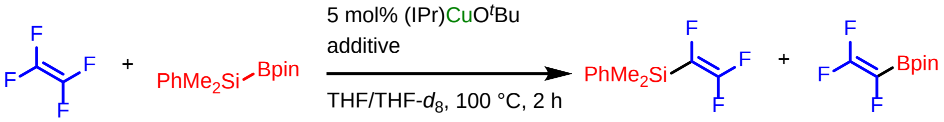


1a: >3 eq **5a** **6a** **7a**

run	*conditions*	^{19}F NMR yield	
1	CuO^{t}Bu (10 mol%) + dppf (10 mol%)	67%	32%
2	CuO^{t}Bu (10 mol%) + BINAP (10 mol%)	0%	0%
3	CuO^{t}Bu (10 mol%) + Xantphos (10 mol%)	58%	30%
4	CuO^{t}Bu (10 mol%) + PPh$_3$ (30 mol%)	5%	0%
5	CuO^{t}Bu (10 mol%) + PCy$_3$ (30 mol%)	59%	4%
6	CuO^{t}Bu (10 mol%) + PCyp$_3$ (30 mol%)	46%	2%
7	CuO^{t}Bu (10 mol%) + P^{i}Pr$_3$ (30 mol%)	59%	2%
8	CuO^{t}Bu (10 mol%) + Phen (10 mol%)	17%	4%
9	(IPr)CuO^{t}Bu (10 mol%)	97%	6%
10	CuO^{t}Bu (10 mol%) + IPr (20 mol%)	7%	5%
11	CuO^{t}Bu (10 mol%) + SIPr (10 mol%)	66%	3%
12	CuO^{t}Bu (10 mol%) + IPrCl (10 mol%)	93%	7%
13[a]	CuO^{t}Bu (10 mol%) + IMes (10 mol%)	70%	2%
14[a]	CuO^{t}Bu (10 mol%) + I^{t}Bu (10 mol%)	trace	trace
15[a]	CuO^{t}Bu (10 mol%) + IPr* (10 mol%)	28%	trace
16[a]	CuO^{t}Bu (10 mol%) + IAd (10 mol%)	3%	4%

[a] 20 h

Table 3.1. Optimization of reaction conditions (ligand)



1a: >3 eq **5a** **6a** **7a**

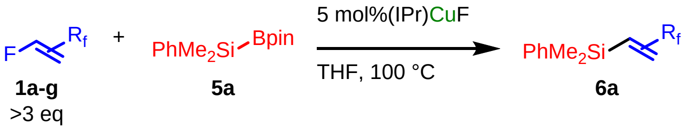
run	additive	^{19}F NMR yield	
1	none	60%	6%
2	5 mol% F-Bpin	79%	3%
3	10 mol% F-Bpin	82%	3%
4	30 mol% F-Bpin	76%	2%
5	50 mol% F-Bpin	78%	2%
6[a]	5 mol% (IPr)CuF	92%	4%
7	10 mol% F-SiMe$_2$Ph	45%	4%
8	10 mol% NEt$_3$	54%	5%
9	10 mol% H-Bpin	42%	8%
10	10 mol% NEt$_3$·3HF	38%	5%
11	10 mol% BF$_3$·OEt$_2$	63%	3%

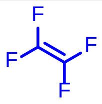
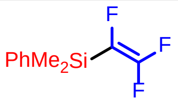
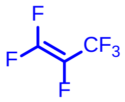
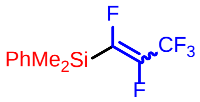
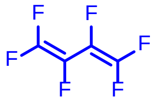
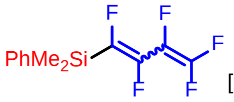
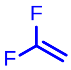
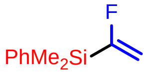
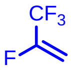
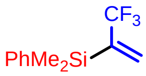
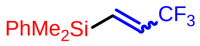
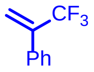
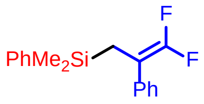
[a] 5 mol% (IPr)CuF was used instead of (IPr)CuO^{t}Bu.

Table 3.2. Optimization of reaction conditions (2)

3.4 Substrate Scope (fluoroalkene)

With the optimal reaction conditions in hand, the scope and limitations of this copper-catalyzed defluorosilylation reaction were examined for a variety of fluoroalkenes (Table 3.3). When hexafluoropropylene (**1b**) was used, the reaction proceeded efficiently and yielded the corresponding mono-defluorosilylated product (**6b**) as a mixture of *E*/*Z* regioisomers (Table 3.3, entry 2). Furthermore, with perfluorobutadiene (**1c**), the corresponding fluorovinylsilane (**6c**) was obtained in moderate yield (entry 3). It is worth noting that polydefluorosilylated products were not generated under excess amount of these polyfluoroalkenes. In addition to these perfluoroalkenes, the use of vinylidene fluoride (**1d**) afforded the respective silylated product (**6d**) in good yield, albeit (IPr)CuO^{t}Bu had to be employed instead of (IPr)CuF (entry 4). Furthermore, trifluoromethylated monofluoroalkenes (**1e** and **1f**) with fluorine atoms at the vinyl and allyl positions were defluorosilylated selectively at the C(sp^2)–F bond to afford silylated products (**6e** and **6f**) respectively, in moderate yield (entries 5 and 6). It should be mentioned that vinyl C–H silylation products were not observed. On the other hand, (3,3,3-trifluoro-1-propen-2-yl)benzene (**1g**) underwent an S$_N$2'-type allylic rearrangement to yield a 3,3-difluoro-2-phenylallylsilane derivative (**6g**) in excellent yield. In contrast, using α,β,β-trifluorostyrene, chlorotrifluoroethylene, perfluoropropoxyethylene, or octafluorocyclopentene did not result in any reaction or side reaction.



Entry	Fluoroalkene	Defluorosilylated product	
1	 **1a**	 **6a**	2 h, 92% (20 h, 85%)
2	 **1b**	 **6b**	20 h, 100% (20 h, 64%) [E/Z = 1/5]
3	 **1c**	 **6c**	5 h, 56% [E/Z = 1/10]
4^b	 **1d**	 **6d**	20 h, 83% (20 h, 77%)
5	 **1e**	 **6e**	5 h, 75% (20 h, 52%)
6	 **1f**	 **6f**	5 h, 69% [E/Z = 1/11]
7^c	 **1g**	 **6g**	5 h, 98% (5 h, 98%)

^{a}Yields determined by ^{19}F NMR spectroscopy; isolated yields given in parentheses; E/Z ratio given in square brackets. ^{b}5 mol% (IPr)CuOtBu was used instead of 5 mol% (IPr)CuF. ^{c}1 eq of 1g and 1.5 eq of 2a were used.

Table 3.3. Substrate Scope

3.4 NMR study

The progress of the catalytic reaction of **1a** with **5a** in the presence of 5 mol% (IPr)CuO^{t}Bu (Table 3.1, run 3) was monitored by ^{19}F NMR spectroscopy, which revealed that **6a** was not formed during the early stages of the reaction (Figure 3.1, A). During this period, only 2-silyl-1,1,2,2-tetrafluoroalkylcopper(I) (**8**; *vide infra*) was generated *in situ* as a possible intermediate. Subsequently, **8** should be generated by 1,2-addition of a silylcopper intermediate to **1a**. The formation of **6a** was observed after 120 min and, ultimately, **6a** was obtained in 60% yield after 320 min. This conversion increase should be induced by F–Bpin generated *in situ* during the defluorosilylation, i,e., upon adding 10 mol% of F–Bpin as an additive, the reaction proceeded immediately (Figure 3.1, B), and the yield of **6a** increased to 82%. This result suggests that F–Bpin plays a key role in facilitating the β-fluorine elimination that leads to (IPr)CuF.

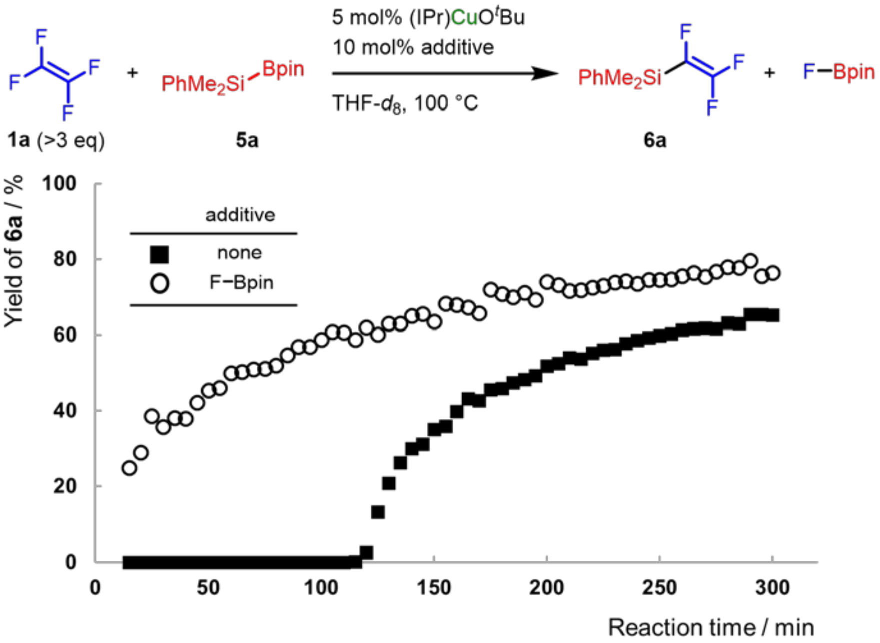
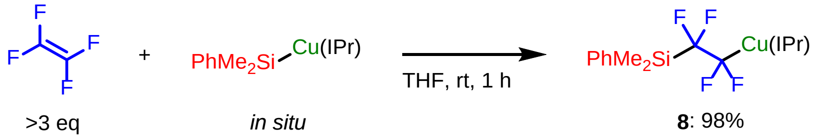


Figure 3.1. Reaction rates in the absence (A: ■; Table 3.1, run 3) and presence (B: ○; Table 1, run 5) of 10 mol% F–Bpin (generated *in situ* from H–Bpin and NEt$_3$·3HF); reactions were monitored by ^{19}F NMR spectroscopy; conditions: Me$_2$PhSi-Bpin (0.10 mmol), TFE (3.5 atm, > 3.0 eq), (IPr)CuO^{t}Bu (0.01 mmol), THF-d_8 (0.5 mL), 100 °C.

3.5 Stoichiometric Reaction

Subsequently, a series of stoichiometric reactions were conducted to gain deeper insight into the reaction mechanism. The structurally well-defined silylcopper(I) complex (IPr)CuSiMe$_2$Ph,[7] prepared *in situ* from the reaction of (IPr)CuO^{t}Bu with **5a**, reacted smoothly with TFE to generate 2-silyl-1,1,2,2-tetrafluoroalkylcopper(I) complex **8** in 98% yield (Scheme 3.2). The molecular structure of **8** was unambiguously determined by single-crystal X-ray diffraction analysis (Figure 3.2).



Scheme 3.2. Synthesis of 2-silyl-1,1,2,2-tetrafluoroalkylcopper(I) complex **8**

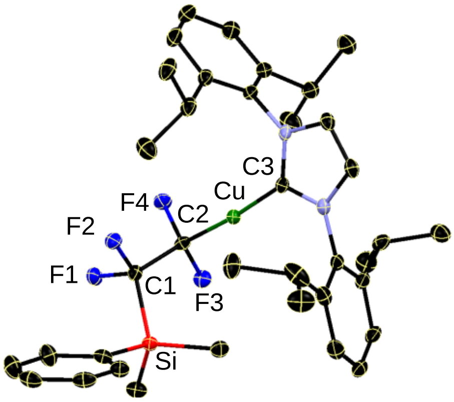
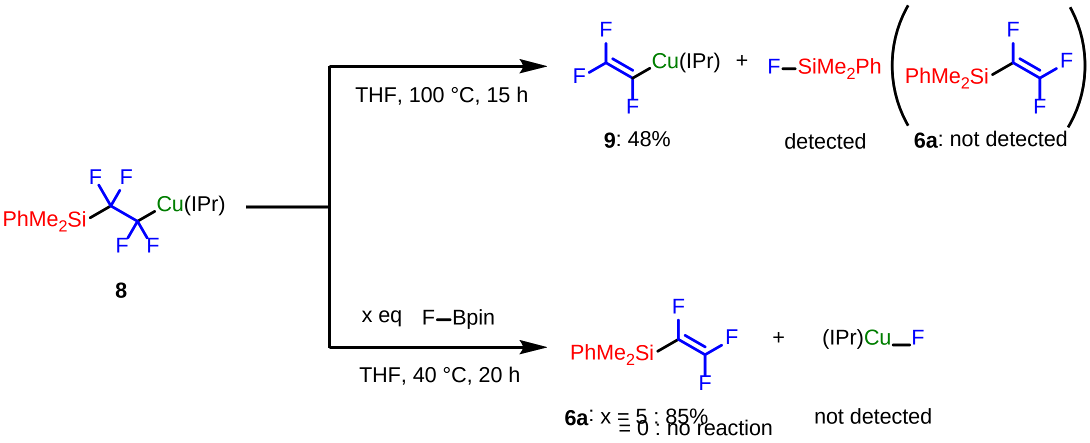


Figure 3.2. ORTEP drawing of **8** with thermal ellipsoids set at 30% probability; hydrogen atoms omitted for clarity, and only selected atoms labelled. Selected bond lengths (Å) and angle (deg): C1–C2 1.522(3), Cu–C2 1.931(2), Cu–C3 1.897(2), C2–Cu–C3 175.16(9).

To clarify the reaction pathway leading to **6a**, as well as the key role of F–Bpin in the catalytic reaction, the reactivity of **8** was investigated further. The thermolysis of **8** in THF at 100 °C afforded trifluorovinylcopper(I) complex **9** in 48% yield instead of the expected catalytic reaction product **6a** (Scheme 3.3, A). The formation of **9** was attributed to a β-fluorine elimination leading to F–$SiMe_2Ph$.[8] The structure of **9** was also unambiguously determined by X-ray diffraction analysis (Figure 3.3). On the other hand, **8** underwent a different type of β-fluorine elimination in the presence of F–Bpin at 40 °C, which afforded **6a** in 85% yield. It is worth noting that **8** remained intact at the same temperature in the absence of F–Bpin (Scheme 3.3, B). This result strongly suggests that the facile formation of **6a** during the catalytic reaction in the presence of F–Bpin is the result of a Lewis-acid-promoted bimolecular β-fluorine elimination.[9,10]



Scheme 3.3. β-fluorine elimination of **8**

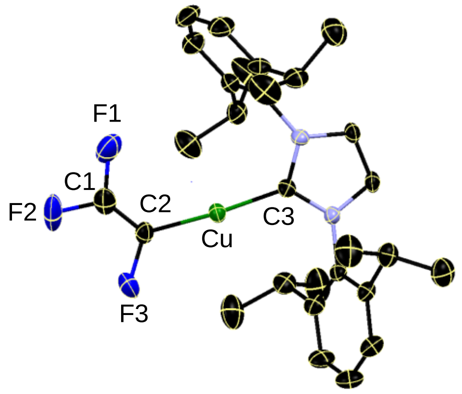
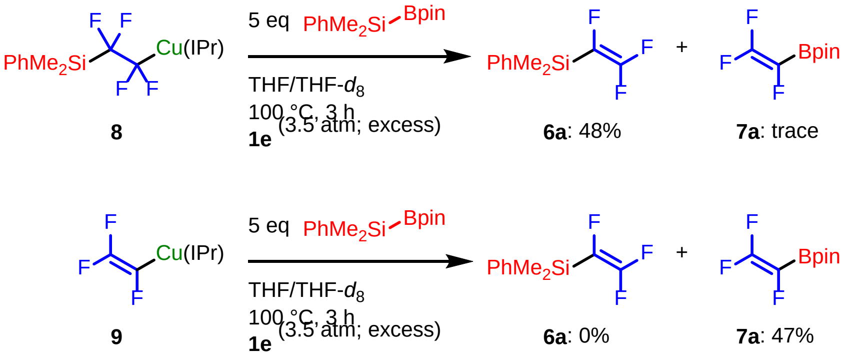


Figure 3.3. ORTEP drawing of **9** with thermal ellipsoids set at 30% probability; hydrogen atoms omitted for clarity, and only selected atoms labelled. Selected bond lengths (Å) and angle (deg): C1–C2 1.276(9), Cu–C2 1.902(6), Cu–C3 1.887(6), C2–Cu–C3 169.3(2), Cu–C2–C1 125.8(5), Cu–C2–F3 121.5(4), C1–C2–F3 111.9(5).

Furthermore, the reactivity of Cu(I) complexes **8** and **9** toward **5a** was examined. In the presence of **1e** as a silylcopper scavenger, the reaction of **8** with **5a** occurred at 100 °C to furnish defluorosilylated **6a** in 48% yield (Scheme 3.4). This result clearly rules out another possible route to **6a** during the catalytic reaction via a transmetallation between **9** and **5a**, i.e., **9** reacts with **5a** to selectively afford the defluoroborylated product **7a** in 47% yield under the same reaction conditions. It is worth noting that only the corresponding defluorosilylated product (**6e**) was observed in both reactions. These results clearly indicate that the silylcopper species is regenerated from the reaction of the

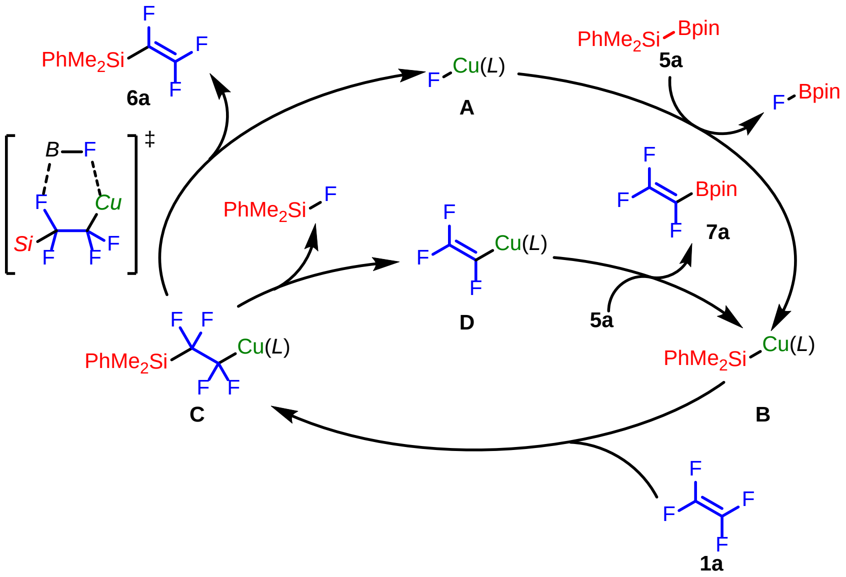
Cu complex with **5a**.



Scheme 3.4. Reactivity of Cu(I) complexes toward **5a**

3.6 A possible reaction mechanism

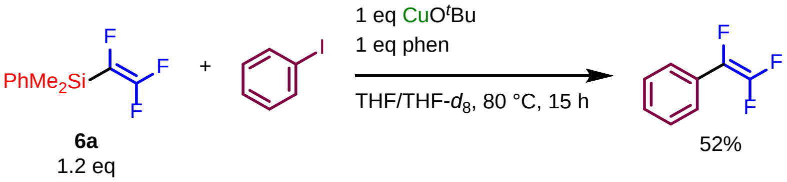
On the basis of the results of the aforementioned stoichiometric experiments, a feasible reaction mechanism is depicted on Scheme 3.5. The transmetallation of copper fluoride **A** with **5a** should afford silylcopper **B** and F–Bpin. Subsequently, the silylcupration of TFE should afford fluoroalkylcopper **C**, under subsequent generation of a deflurosilylated product and regeneration of the copper fluoride species upon β-fluorine elimination promoted by F–Bpin. However, in the case where β-fluorine elimination affords a fluorosilane, fluorovinylcoppper **D** should be generated, which would react with **5a** to afford a silylcopper and a defluoroborylated product.



Scheme 3.5. A possible reaction mechanism

3.7 Transformation of trifluorovinylsilane

The thus obtained silylated products may also serve as useful synthetic units for the introduction of fluoroalkene moieties (Scheme 3.6).[11] For example, the copper-mediated cross-coupling reaction of trifluorovinylphenyldimethylsilane (**6a**) with iodobenzene furnished α,β,β-trifluorostyrene in moderate yield.



Scheme 3.6. Coupling reaction of **6a** with iodobenzene

3.8 Conclusion

In chapter 3, the copper-catalyzed defluorosilylation reaction of fluoroalkenes with silylborane is described. The mechanistic studies indicate that the key steps of this defluorosilylation reaction are the 1,2-addition of a silylcopper intermediate to the polyfluoroalkene, and a subsequent β-fluorine elimination leading to the corresponding vinylsilane and the regenerated copper(I) fluoride. The role of F–Bpin, which is generated *in situ* during the defluorosilylation, was revealed to facilitate the β-fluorine elimination.

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Chem. **1989**, *367*, 1.

3.10 Experimental section

Preparation of (IPr)CuF

(IPr)CuF was prepared according to the literature[S1] with a minor modification.

Under N_2 atmosphere, a THF solution (20 mL) of (IPr)CuO^{t}Bu (526 mg, 1.00 mmol) and PhCOF (186 mg, 1.50 mmol, 1.5 equiv) was stirred at room temperature for 1 h. After the removal of the solvent, the residue was washed with *n*-pentane (ca. 5 mL) several times to afford (IPr)CuF (457 mg, 0.97 mmol, 97%) as a colorless powder,

^{1}H NMR (400 MHz, THF-d_8, 22 °C, δ/ppm): 1.22 (d, *J* = 6.9 Hz, 12H), 1.31 (d, *J* = 6.9 Hz, 12H), 2.63 (sept, *J* = 6.9 Hz, 4H), 7.34 (d, *J* = 7.7 Hz, 4H), 7.47 (s, 2H), 7.48 (t, *J* = 7.7 Hz, 2H);

^{19}F NMR (376 MHz, THF-d_8, 22 °C, δ/ppm): –247.3

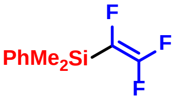
The chemical shifts were consistent with those reported in the literature.[S2]

General procedure A (for monitoring of the reaction by ^{19}F NMR, Table 3.1)

To a solution of a copper salt, a ligand, and an additive in THF/THF-d_8 (0.50 mL, v/v′ = 4/1) were added Me_2PhSi-Bpin (**5a**, 26.3 mg, 0.100 mmol) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7; recommended maximum pressure 150 psi = 10 atm), charged with TFE (**1a**, 3.5 atm, an excess amount) as a gas, and heated. Monitoring the reaction was performed by means of ^{19}F NMR spectroscopy. The yields of the defluorosilylated product **6a** and the defluoroborylated product **7a** were determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard.

General procedure B (for isolation of 6): The reactions were conducted with an autoclave reactor. A mixture of Me_2PhSi-Bpin (**5a**, 263 mg, 1.00 mmol, 1 equiv) and (IPr)CuF (23.6 mg, 0.05 mmol, 0.05 equiv) was dissolved in 5.0 mL of THF. The resulting solution was transferred into the autoclave reactor, and then fluoroalkenes gas **1** (3.5 atm) was charged. The reaction mixture was heated at 100 ºC for 20 h. After the unreacted **1** was purged from the reactor (***caution***: The reaction mixture must be handled in a well-ventilated fume hood.), the reaction mixture was concentrated *in vacuo*. 10.0 mL of pentane was added to the residue, and the resulting suspension was filtered through a short silica column. The filtrate was concentrated *in vacuo* to yield the desired defluorosilylated product **6**.

dimethyl(phenyl)(1,2,2-trifluorovinyl)silane (6a)



Following the general procedure B, TFE (**1a**) was converted into the title compound (184 mg, 85%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, 22 °C, δ/ppm): 0.53 (s, 6H), 7.38-7.59 (m, 5H);

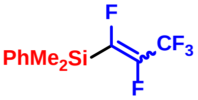
^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, 22 °C, δ/ppm): –4.13, 128.3, 130.2, 132.7 (ddd, J_{CF} = 137.8, 68.9, 66.7 Hz), 133.9, 134.3, 137.9 (ddd, J_{CF} = 317.5, 277.7, 39.8 Hz);

^{19}F NMR (376 MHz, $CDCl_3$, 22 °C, δ/ppm): –200.3 (dd, J_{FF} = 116.5, 24.8 Hz, 1F), –117.5 (dd, J_{FF} = 116.5, 65.5 Hz, 1F), –89.0 (dd, J_{FF} = 65.5, 24.8 Hz, 1F);

HRMS Calcd for $C_{10}H_{11}F_3Si$ 216.0582, found *m/z* 216.0581.

The chemical shifts were consistent with those reported in the literature.[S3]

dimethyl(perfluoroprop-1-en-1-yl)(phenyl)silane (6b)



Following the general procedure B, HFP (**1b**) was converted into the title compound (170 mg, 64%) as a colorless oil. **6b** was isolated as a mixture of *E*/*Z* regioisomers (*E*/*Z* = 1/5).

Spectrum for (*Z*)-dimethyl(perfluoroprop-1-en-1-yl)(phenyl)silane

^{1}H NMR (400 MHz, $CDCl_3$, 22 °C, δ/ppm): 0.58 (s, 6H), 7.26-7.58 (m, 5H);

^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, 22 °C, δ/ppm): –4.32 (dd, J_{CF} = 3.0, 3.0 Hz), 118.6 (qd, J_{CF} = 273.5, 38.7 Hz), 128.4, 130.6, 133.0, 134.1, 149.7 (dm, J_{CF} = 238.3 Hz), 161.5 (dd, J_{CF} = 285.1, 62.7 Hz);

^{19}F NMR (376 MHz, $CDCl_3$, 22 °C, δ/ppm): –166.0 (dq, J_{FF} = 136.3, 3.5 Hz, 1F), –156.5 (dq, J_{FF} = 136.3, 21.2 Hz, 1F), –68.0 (dd, J_{FF} = 21.2, 3.5 Hz, 3F);

HRMS Calcd for $C_{11}H_{11}F_5Si$ 266.0550, found *m/z* 266.0546 (as an *E*/*Z* mixture).

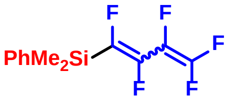
Spectrum for (*E*)-dimethyl(perfluoroprop-1-en-1-yl)(phenyl)silane

^{1}H NMR (400 MHz, $CDCl_3$, 22 °C, δ/ppm): 0.56 (s, 6H), 7.26-7.58 (m, 5H);

^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, 22 °C, δ/ppm): –3.3 (br s), 128.3, 130.5, 132.7, 133.9, The peaks assignable to the $CF_3CF=CF$ moiety were not distinctly observed due to their multiple coupling.;

^{19}F NMR (376 MHz, $CDCl_3$, 22 °C, δ/ppm): –140.4 (dq, J_{FF} = 14.2, 14.2 Hz, 1F), –136.2 (dq, J_{FF} = 14.2, 5.8 Hz, 1F), –67.3 (dd, J_{FF} = 14.2, 5.8 Hz, 3F).

dimethyl(perfluorobuta-1,3-dien-1-yl)(phenyl)silane (6c)



Following the modified general procedure A, 1,3-perfluorobutadiene (**1c**, 1.0 atm, an excess amount) was converted into the title compound (56%) as a mixture of *E*/*Z* regioisomers (*E*/*Z* = 1/10).

After determining the yield and the *E*/*Z* ratio, the solvents were removed under reduced pressure and the residue was extracted with *n*-hexane (ca. 3 mL). The extract was passed through a short silica column. The filtrate was concentrated under reduced pressure. To the residue was added $CDCl_3$ to obtain the ^{1}H and ^{19}F NMR spectra;

Spectrum for (*Z*)-dimethyl(perfluorobuta-1,3-dien-1-yl)(phenyl)silane

^{1}H NMR (400 MHz, $CDCl_3$, 22 °C, δ/ppm): 0.57 (s, 6H), 7.39-7.58 (m, 5H);

^{19}F NMR (376 MHz, $CDCl_3$, 22 °C, δ/ppm): –182.8 (ddd, J_{FF} = 113.5, 33.5, 12.0 Hz, 1F), –157.0 (ddd, J_{FF} = 139.6, 33.5, 13.1 Hz, 1F), –150.9 (ddd, J_{FF} = 139.6, 12.0, 7.8 Hz, 1F), –106.2 (dddd, J_{FF} = 113.5, 49.9, 22.9, 13.1 Hz, 1F), –94.8 (ddm, J_{FF} = 49.9, 33.5 Hz, 1F);

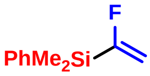
HRMS Calcd for $C_{12}H_{11}F_5Si$ 278.0550, found *m/z* 277.0468 (as an *E*/*Z* mixture).

Spectrum for (*E*)-dimethyl(perfluorobuta-1,3-dien-1-yl)(phenyl)silane

^{1}H NMR (400 MHz, $CDCl_3$, 22 °C, δ/ppm): 0.52 (s, 6H), 7.39-7.58 (m, 5H);

^{19}F NMR (376 MHz, $CDCl_3$, 22 °C, δ/ppm): –172.0 (dddd, J_{FF} = 119.7, 37.2, 28.5, 3.7 Hz, 1F), –131.8 (dd, J_{FF} = 24.9, 3.7 Hz, 1F), –123.6 (dddd, J_{FF} = 37.2, 24.9, 17.5, 5.1 Hz, 1F), –106.5 (ddd, J_{FF} = 119.7, 49.0, 17.5 Hz, 1F), –92.5 (ddm, J_{FF} = 49.0, 28.5 Hz, 1F).

(1-fluorovinyl)dimethyl(phenyl)silane (6d)



Following the modified general procedure B in which (IPr)CuO^{t}Bu (26.3 mg, 0.050 mmol, 0.050 equiv) was used instead of (IPr)CuF, VdF (**1d**) was converted into the title compound (136.2 mg, 77%) as a colorless oil.

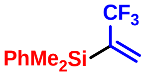
^{1}H NMR (400 MHz, $CDCl_3$, 22 °C, δ/ppm): 0.50 (m, 6H), 4.85 (dm, J_{HF} = 61.6 Hz), 5.40 (dm, J_{HF} = 32.9 Hz), 7.40-7.65 (m, 5H);

^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, 22 °C, δ/ppm): –3.9, 107.2 (d, J_{CF} = 8.0 Hz), 128.1, 129.9, 134.1, 135.3, 174.5 (d, J_{CF} = 281.7 Hz);

^{19}F NMR (376 MHz, $CDCl_3$, 22 °C, δ/ppm): –103.7 (ddd, J_{HF} = 61.6, 32.9 Hz, 1F);

HRMS Calcd for $C_{11}H_9F_3Si$ 180.0771, found *m/z* 180.0776.

dimethyl(phenyl)(3,3,3-trifluoroprop-1-en-2-yl)silane (6e)



Following the general procedure B, HFO-1234yf (**1e**) was converted into the title compound (119.2 mg, 52%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$, 22 °C, δ/ppm): 0.53 (s, 6H), 5.78 (m, 1H), 6.43 (m, 1H), 7.39-7.58 (m, 5H);

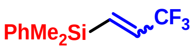
^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, 22 °C, δ/ppm): –2.79, 125.9 (q, J_{CF} = 272.7 Hz), 128.1, 129.9, 134.2, 134.4 (q, J_{CF} = 8.5 Hz), 135.7, 141.0 (q, J_{CF} = 29.7 Hz);

^{19}F NMR (376 MHz, $CDCl_3$, 22 °C, δ/ppm): –64.3 (s, 3F);

HRMS Calcd for $C_{11}H_9F_3Si$ 230.0739, found *m/z* 230.0742.

The chemical shifts were consistent with those reported in the literature.[S4]

dimethyl(phenyl)(3,3,3-trifluoroprop-1-en-1-yl)silane (6f)



Following the modified general procedure A, HFO-1234ze (**1f**) was converted into the title compound (69%) as a mixture of *E*/*Z* regioisomers (*E*/*Z* = 1/11).

After determining the yield and the *E*/*Z* ratio, the solvents were removed under reduced pressure and the residue was extracted with *n*-hexane (ca. 3 mL). The extract was passed through a a short silica column. The filtrate was concentrated under reduced pressure. To the residue was added $CDCl_3$ to obtain the ^{1}H and ^{19}F NMR spectra;

Spectrum for (*Z*)-dimethyl(phenyl)(3,3,3-trifluoroprop-1-en-1-yl)silane

^{1}H NMR (400 MHz, $CDCl_3$, 22 °C, δ/ppm): 0.46 (s, 6H), 6.34-6.47 (m, 2H), 7.36-7.53 (m, 5H);

^{19}F NMR (376 MHz, $CDCl_3$, 22 °C, δ/ppm): –61.3 (d, J_{HF} = 6.5 Hz, 1F);

HRMS Calcd for $C_{11}H_{13}F_3Si$ 230.0739, found *m/z* 230.0739 (as an *E*/*Z* mixture).

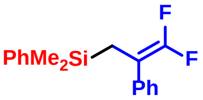
The chemical shifts were consistent with those reported in the literature.[S5]

Spectrum for (*E*)-dimethyl(phenyl)(3,3,3-trifluoroprop-1-en-1-yl)silane

^{1}H NMR (400 MHz, $CDCl_3$, 22 °C, δ/ppm): 0.43 (s, 6H), 6.0 (dq, J_{HH} = 18.9 Hz, J_{HF} = 5.4 Hz, 1H), 6.76 (dq, J_{HH} = 18.9 Hz, J_{HF} = 2.4 Hz, 1H), 7.36-7.53 (m, 5H);

^{19}F NMR (376 MHz, $CDCl_3$, 22 °C, δ/ppm): –66.4 (d, J_{HF} = 5.4 Hz, 1F).

(3,3-difluoro-2-phenylallyl)dimethyl(phenyl)silane (6g)



To a solution of (IPr)CuF (7.8 mg, 0.015 mmol, 0.050 equiv) in THF/THF-*d*$_8$ (0.50 mL, v/v′ = 4/1) were added **5a** (118.4 mg, 0.45 mmol, 1.5 equiv) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a J-Young tube, and then (3,3,3-trifluoroprop-1-en-2-yl)benzene (**1g**, 51.6 mg, 0.30 mmol, 1 equiv) was added. The reaction mixture was heated at 100 °C for 5 h. Monitoring the reaction was performed by means of ^{19}F NMR spectroscopy. The reaction mixture was concentrated *in vacuo*. Pentane (5.0 mL) was added to the residue, and the resulting suspension was filtered through a short silica column. The filtrate was concentrated *in vacuo*. The title compound (85.4 mg, 98%) was isolated as a colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$, 22 °C, δ/ppm): 0.14 (s, 6H), 1.96 (dd, J_{HF} = 3.1, 2.1 Hz 2H), 7.19-7.44 (m, 10H);

^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, 22 °C, δ/ppm): –2.8, 16.6, 90.1 (dd, J_{CF} = 23.5, 15.0 Hz), 127.3, 127.9, 128.4, 128.5 (dd, J_{CF} = 3.4, 3.4 Hz), 133.6, 135.1 (dd, J_{CF} = 5.3, 3.7 Hz), 138.3, 152.8 (dd, J_{CF} = 288.7, 285.0 Hz);

^{19}F NMR (376 MHz, $CDCl_3$, 22 °C, δ/ppm): –94.4 (d, J_{FF} = 47.9 Hz, 1F), –117.0 (dt, J_{FF} = 47.9 Hz, J_{HF} = 3.1 Hz, 1F);
HRMS Calcd for $C_{17}H_{18}F_2Si$ 288.1146, found *m/z* 288.1145.

Plotting the yield of 6a against reaction time in the Cu(I)-catalyzed defluorosilylation reaction of TFE with Me_2PhSi-Bpin. (Figure 3.1)

The reactions were conducted with a pressure-tight NMR tube. A mixture of Me_2PhSi-Bpin (**5a**, 26.3 mg, 0.100 mmol, 1 equiv) and (IPr)CuO^{t}Bu (2.63 mg, 0.005 mmol) was dissolved in 0.50 mL of THF-d_8. The resulting solution was transferred into the tube, and then TFE (3.5 atm, >0.30 mmol) was charged into the tube. The reaction mixture was heated at 100 ºC until the reaction was terminated. Monitoring the reaction and determination of the yield were performed by means of ^{19}F NMR spectroscopy at 100 °C five minutes each.

Stoichiometric reactions (Scheme 3.3-3.5)

Reaction of TFE (1a) with 5a in the presence of (IPr)CuO^{t}Bu (Scheme 3.3)

To a solution of (IPr)CuO^{t}Bu (5.26 mg, 0.02 mmol, 1 equiv) in THF/THF-d_8 (0.50 mL, v/v′ = 4/1) were added Me_2PhSi-Bpin (**5a**, 5.26 mg, 0.02 mmol, 1.0 equiv) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7), and then TFE (**1a**, 3.5 atm, the excess amount) was charged as a gas. The reaction mixture was stirred at room temperature for 1 h. The yield of **8** was determined by ^{19}F NMR spectroscopy using α,α,α-trifluorotoluene as an internal standard.

Isolation of $Me_2PhSiCF_2CF_2Cu(IPr)$ (8): The reaction was conducted with an autoclave reactor. A mixture of (IPr)CuO^{t}Bu (263 mg, 0.50 mmol), and **5a** (131 mg, 0.50 mmol) was dissolved in 5.0 mL of THF. The resulting solution was transferred into an autoclave reactor, and then TFE (3.5 atm) was charged into the reactor. The reaction mixture was stirred at room temperature. for 1 h. After the unreacted TFE was purged from the reactor (***caution***: The reaction mixture must be handled in a well-ventilated fume hood.), the reaction mixture was concentrated *in vacuo*. The residue was washed with 5 mL of hexane several-times. The title compound **8** was isolated as a white solid (337 mg, 0.49 mmol, 98%). A single crystal suitable for X-ray diffraction analysis was prepared by recrystallization from toluene /hexane at 22 °C.

^{1}H NMR (400 MHz, THF-*d*$_8$, 22 °C, δ/ppm): 0.17 (s, 6H), 1.20 (d, J_{HH} = 6.8 Hz, 12H, CH-C*H*$_3$), 1.28 (d, J_{HH} = 6.8 Hz,12H), 2.61 (sept, J_{HH} = 6.8 Hz, 4H), 7.15–7.46 (m, 13H);

^{19}F NMR (376 MHz, THF-*d*$_8$, 22 °C, δ/ppm): –122.0 (m, 2F), –112.2 (m, 2F);

^{13}C{^{1}H} NMR (100.6 MHz, THF-*d*$_8$, 22 °C, δ/ppm): –4.21, 23.8, 29.4, 124.2, 124.5, 127.7, 129.4, 130.7, 135.1, 135.6, 136.5, 146.4, 183.3, The peaks assignable to the CF_2CF_2 moiety were not distinctly observed due to their multiple coupling.;

Anal. Calcd for $C_{37}H_{48}F_4SiN_2Cu$: C, 64.55; H, 7.03; N, 4.07. Found: C, 64.75; H,7.49; N, 4.02

Thermolysis of fluoroalkylcopper(I) 8 (Scheme 3.4A)

A solution of **8** (13.8 mg, 0.02 mmol) in THF/THF-*d*$_8$ (v/v' = 4/1) (0.5 mL) was transferred into a J-Young NMR tube and heated at 100 °C. Formation of **9** was confirmed by ^{19}F NMR analysis and the yield (0.0096 mmol, 48%) was determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard. In the reaction mixture, the generation of $FSiMe_2Ph$ was detected (^{19}F NMR: δ –164.3 ppm in THF-*d*$_8$)

Spectrum for **9**;

^{19}F NMR (376 MHz, THF/THF-*d*$_8$, 22 °C, δ/ppm): –195.2 (dd, J_{FF} = 32.8, 97.0 Hz, 1F), –138.2 (dd, J_{FF} = 97.0, 97.0 Hz, 1F), –102.3 (dd, J_{FF} = 32.8, 97.0 Hz, 1F).

The chemical shifts were consistent with those reported in the literature.

Reaction of 8 with F-Bpin (Scheme 3.4B)

To a solution of **8** (13.8 mg, 0.02 mmol) in THF/THF-*d*$_8$ (0.40 mL, v/v′ = 4/1) were added ca. 1 M F-Bpin THF solution that was prepared from H–Bpin and $NEt_3·3HF$ (0.10 mL, ca. 0.1 mmol, ca. 5.0 equiv) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a J-Young tube. The reaction mixture was heated at 40 °C for 20 h. Formation of **6a** was confirmed by ^{19}F NMR analysis and the yield (0.017 mmol, 85%) was determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard.

Reaction of copper complexes (8 and 9) with 5a (Scheme 3.5)

To a solution of **8** or **9** (0.02 mmol) in THF/THF-d_8 (0.50 mL, v/v′ = 4/1) were added Me_2PhSi-Bpin (**5a**, 26.2 mg, 0.1 mmol, 5.0 equiv) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7), and then 2,3,3,3-tetrafluoropropene (**1e**, HFO-1234yf, 3.5 atm, an excess amount) was charged as a gas. The reaction mixture was heated at 100 °C for 1 h. Formation of **6a** (or **7a**) was confirmed by ^{19}F NMR analysis. The yields of them were determined by ^{19}F NMR spectroscopy using α,α,α-trifluorotoluene as an internal standard.

Copper-mediated arylation of 6a (Scheme 3.7)

To a solution of **6a** (13.0 mg, 0.06 mmol, 1.2 equiv) were added CuO^{t}Bu (6.8 mg, 0.05 mmol, 1.0 equiv), 1,10-phen (9.0 mg, 0.05 mmol, 1.0 equiv), iodobenzene (10.2 mg, 0.05 mmol, 1 equiv) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a J-Young tube. The reaction mixture was heated at 80 °C for 15 h. Formation of 1-trifluoromethyl-4-(1,2,2-trifuluorovinyl)benzene was confirmed by ^{19}F NMR analysis and GCMS analyses, and the yield (0.026 mmol, 52%) was determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard.

^{19}F NMR (376 MHz, THF/THF-d_8, 22 °C, δ/ppm): –178.6 (dd, J_{FF} = 108.8, 32.0 Hz, 1F), –117.0 (dd, J_{FF} = 108.8, 70.6 Hz, 1F), –103.4 (dd, J_{FF} = 70.6, 32.0 Hz, 1F);

MS (EI): *m/z* (%): 158 (100) [M]+, 107 (28).

Spectral data of 1-trifluoromethyl-4-(1,2,2-trifuluorovinyl)benzene were identical to that previously reported.[S6]

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Chapter 4

Cu(I)-Catalyzed Defluoroborylation of Polyfluoroalkenes

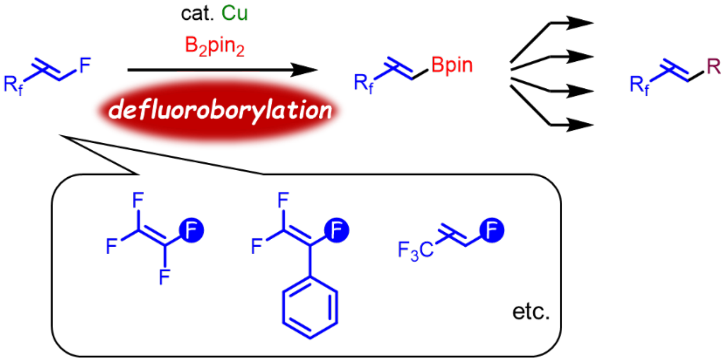
4.1 Introduction

Defluoroborylation, a borylative cleavage of C–F bond of polyfluorocompounds, has been regard as a powerful tool to access fluorinated organoboron compounds. The resulting borylated compounds are expected to serve as useful synthetic intermediates that take advantage of reliable transformations based on versatile well-established organoboron chemistries.[1] Recently, defluroborylation reactions of fluoroarenes were developed by several groups.[2] In 2015, Zhang *et al*. developed the first example of an *ortho*-selective defluoroborylation of polyfluoroarenes with a Rh catalyst.[2a] In 2015, Martin *et al.* described the Ni-catalyzed defluoroborylation of monofluoroarenes.[2b] Contemporaneously, Niwa and Hosoya *et al.* independently established an efficient method for the synthesis of various borylarenes via the Ni/Cu catalyzed defluoroborylation of monofluoroarenes.[2c] In 2016, Marder and Radius et al. reported a complementary methods for defluoroborylation of polyfluoroarenes employing Ni(IMes)$_2$ as a catalyst.[2d] Furthermore, in 2017, Niwa and Hosoya *et al.* achieved the Cu catalyzed defluoroborylation of polyfluoroarenes.[2e] However, its application to fluoroalkenes has been unexplored thus far except for an S$_N$2'-type allylic rearrangement reaction of fluoroalkenes.[3]

As described in chapter 3, Cu(I)-catalyzed defluorosilylation of polyfluoroalkenes has been developed.[4] Based on the previous study, the idea of employing diboron reagents instead of silylborane reagents was conceived to achieve defluoroborylation of fluoroalkenes. It should be mentioned that several groups have also disclosed copper-catalyzed transformations of fluoroalkenes that involve borylcupration and β-fluorine elimination steps at the almost same time.[5]

Described in this chapter is a practical synthetic method for a diverse range of fluorinated vinylborane, which has been achieved based on the copper-catalyzed regioselective borylative cleavage of C–F bond in various polyfluoroalkenes (Scheme

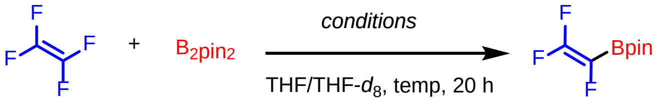
4.1).



Scheme 4.1. Fluorinated vinylboranes synthesis from the copper-catalyzed defluoroborylation of polyfluoroalkenes

4.2 Development of the catalytic reaction

In the presence of 10 mol% (IPr)CuO^{t}Bu as a catalyst, the reaction of B_2pin_2 (**10a**) with TFE (**1a**) at 100 °C afforded the desired borylated product **7a** quantitatively (Table 4.1, run 1). Using the pre-synthesized complex was important to achieve an efficient conversion; significant decrease in the yield of **7a** was observed when a mixture of (IPr)CuCl and sodium *tert*-butoxide was used (runs 2 and 3). The amount of the catalyst could be reduced to 5 mol %, which still afforded **7a** in an excellent yield (run 4). Moreover, the reaction could be conducted at lower temperatures by extending the reaction time, which afforded **7a** in acceptable yields (runs 5–7).



1a (>3 eq) **10a** **7a**

run	*conditions*	temp	^{19}F NMR yield
1	10 mol% (IPr)CuO^{t}Bu	100 °C	100%
2	10 mol% (IPr)CuCl, 10 mol% NaO^{t}Bu	100 °C	37%
3	10 mol% (IPr)CuCl, 100 mol% NaO^{t}Bu	100 °C	16%
4	5 mol% (IPr)CuO^{t}Bu	100 °C	93%
5	5 mol% (IPr)CuO^{t}Bu	80 °C	77% (90%)^a
6	5 mol% (IPr)CuO^{t}Bu	60 °C	58% (89%)^b
7	5 mol% (IPr)CuO^{t}Bu	40 °C	22% (69%)^b

^{a} 80 h, ^{b} 240 h

Table 4.1. Optimization of reaction condition

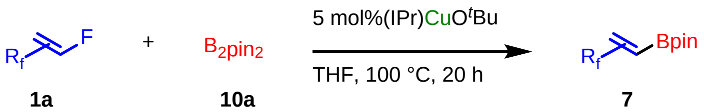
4.3 Substrate Scope

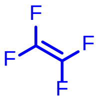
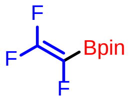
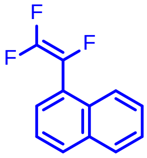
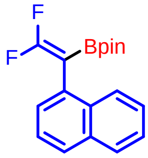
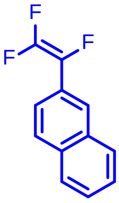
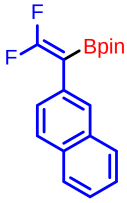
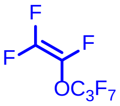
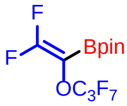
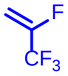
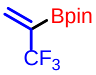
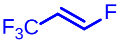
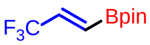
The optimized conditions for monodefluoroborylation of TFE (**1a**) could be applied to monodefluoroborylation of several polyfluoroalkenes, including (tifluorovinyl)arenes and trifluoromethylated monofluoroalkenes (Table 4.2). Because of the water sensitivity of the products, structure identification and determination of the yields of products other than **7i** were conducted by ^{19}F NMR analysis. The reactions of 1- and 2-(trifluorovinyl)naphthalene (**1h** and **1i**) proceeded selectively at the geminal position with respect to the aryl group to give **7h** and **7i** (entries 2 and 3). The reaction with heptafluoropropyl trifluorovinyl ether (**1j**) afforded only a trace amount of the desired product (**7j**), and trifluorovinylborane (**7a**) was obtained in 7% yield (entry 4). This result indicated that β-alkoxy elimination preferably occurred compared with the desired β-fluorine elimination. In this case, the desired **7j** was obtained in moderate yield using xantphos as the ligand. In addition to these polyfluoroalkenes, trifluoromethylated monofluoroalkenes (**1e** and **1f**), which have fluorine atoms at the vinyl and allyl positions, respectively, were monodefluoroborylated selectively at the C(sp^2)–F bond moiety to afford borylated products **7e** and **7f** in high yields (entries 5 and 6).

4.4 Stoichiometric Reaction

Several stoichiometric reactions offered an insight into the reaction mechanism (Scheme 4.2). The reaction of the structurally characterized borylcopper(I) complex (IPr)CuBpin,[6] which was prepared by mixing (IPr)CuO^{t}Bu and B$_2$pin$_2$ (**10a**) in situ, with an excess amount of TFE (**1a**) in THF at room temperature afforded a trifluorovinylcopper(I) complex **9** in 91% yield within a few minutes. (Scheme 4.2 A). In this reaction, generation of fluoroboronate (F–Bpin) was also observed, indicating that **9** was formed via 1,2-addition of the borylcopper(I) complex to **1a** followed by elimination of F–Bpin, which was promoted by the thermodynamically favored B–F bond formation. Furthermore, any other intermediates, including the expected borylcupration complex, pinBCF$_2$CF$_2$Cu(IPr) (**11**), were not detected during the reaction. Such a transient behavior of **11** stands in stark contrast to the thermal stability of the silylcupration analogue Me$_2$PhSiCF$_2$CF$_2$Cu(IPr) (**8**).[4] It is necessary for the progress of β-fluorine elimination of

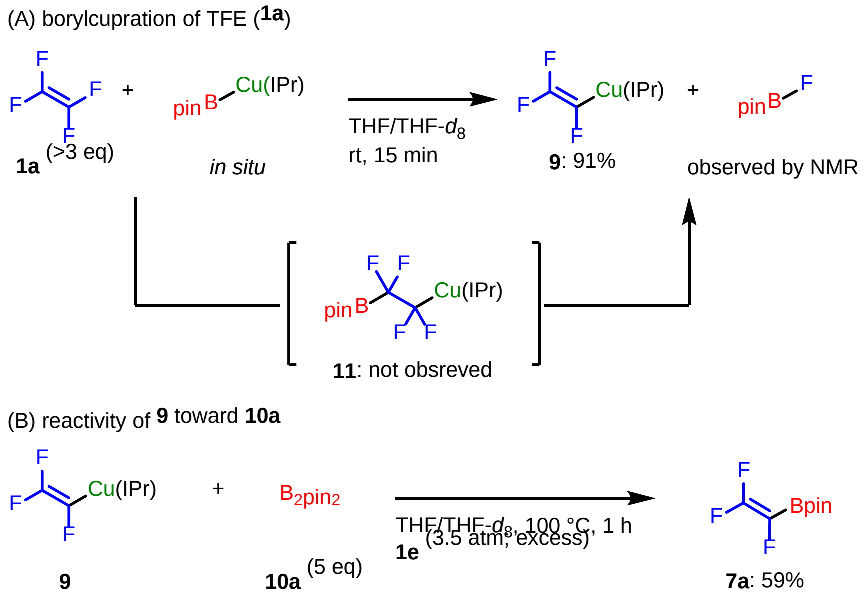
8 to be heated at 100 °C. The differences in reactivity between **8** and **11** toward the β-fluorine elimination leading to **9** may reflect differences in the fluorophilicity of the SiMe2Ph and Bpin moieties. The reaction of isolated **9** with diboron **10a** in the presence of **1e**, which was used as a borylcopper scavenger, proceeded at 100 °C to afford trifluorovinylborane **7a** in 60% yield (Scheme 4.2 B). In this reaction, formation of the borylated product **7e** was also observed, indicating that the borylcopper species was regenerated during the reaction.



Entry	Fluoroalkene	Defluoroborylated product	
1[a]	 **1a**	 **7a**	93%
2[b]	 **1h**	 **7h**	21%
3[b]	 **1i**	 **7i**	50%
4[c]	 **1j**	 **7j**	1 (+ **7a** 7%) 37%[d]
5[a]	 **1e**	 **7e**	65%
6[a,c]	 **1f**	 **7f**	87%

Yields were determined by ^{19}F NMR. [a]Excess amount of fluoroalkene gases were used. [b]1.5 equiv of B_2pin_2 was used. [c]3 equiv of **1j** was used. [d]CuO^{t}Bu (5 mol%) and xantphos (5 mol%) were used instead of (IPr)CuO^{t}Bu.

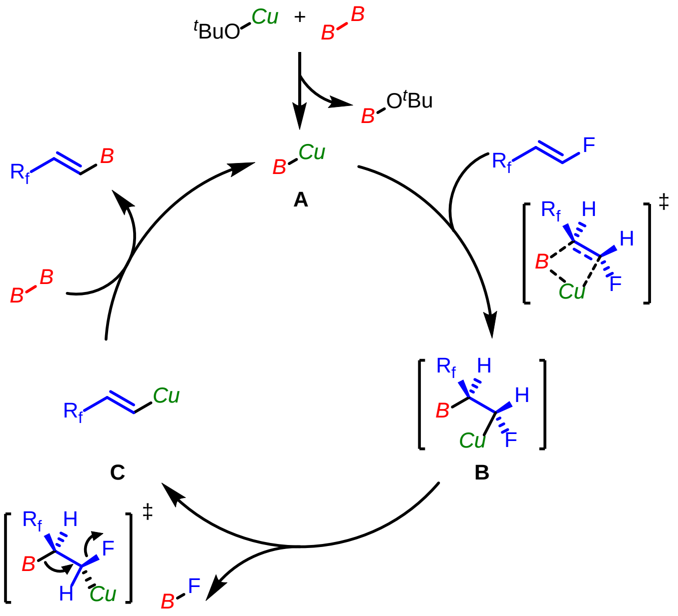
Table 4.2. Substrate scope



Scheme 4.2. Stoichiometric reactions

4.5 A possible reaction mechanism

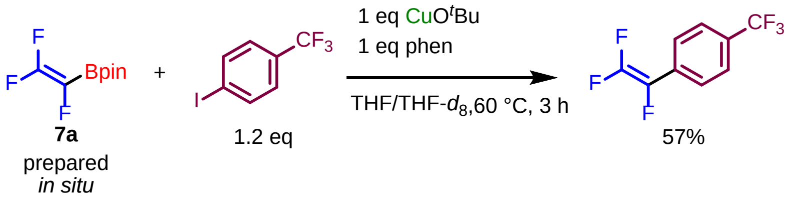
On the basis of the results of the aforementioned stoichiometric experiments, a feasible reaction mechanism is depicted on Scheme 4.3. The transmetallation of CuO^{t}Bu with diboron **10a** should afford a borylcopper **A**. Subsequently, the *syn*-borylcupration[7] of polyfluoroalkene should afford fluoroalkylcopper **B**, under subsequent generation of a fluorovinylcoppper **C** upon *anti*-β-fluorine elimination leading to F–Bpin. Then, **C** would react with **10a** to regenerate a borylcopper **A** and a defluoroborylated product.



Scheme 4.3. A possible reaction mechanism

4.6 Transformation of trifluorovinylborane

The borylated products served as useful synthetic units for introduction of fluoroalkene moieties (Scheme 4.4). For example, copper-mediated cross-coupling reaction of trifluorovinylborane (**7a**) with 4-iodobenzotrifluoride proceeded smoothly to give a trifluorostyrene derivative.



Scheme 4.4. Coupling reaction of 7**a** with 4-iodobenzotrifluoride

4.7 Conclusion

In chapter 4, a practical synthetic method for borylated fluoroalkenes via copper-catalyzed defluoroborylation of polyfluoroalkenes is described. The method has been successfully applied to a broad range of substrates, including tetrafluoroethylene (TFE), (tifluorovinyl)arenes, and trifluoromethylated monofluoroalkenes. Stoichiometric experiments indicate that the key steps of this defluoroborylation reaction are: i) the 1,2-addition of a borylcopper intermediate to the polyfluoroalkene, ii) a subsequent selective anti-β-fluorine elimination leading to a fluorovinylcopper intermediate and a fluoroborane species, and iii) a transmetalation between the fluorovinylcopper and a diboron reagent to afford defluoroborylated product and regenerate a borylcopper,.

4.8 References and notes

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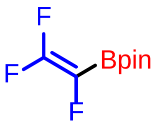
4.9 Experimental section

Procedure for optimization study of copper-catalyzed defluoroborylation of 1a (Table 4.1)

To a solution of a copper salt, a ligand, and a base in THF/THF-d_8 (0.50 mL, v/v′ = 4/1) were added (Bpin)$_2$ (**10a**, 25.4 mg, 0.100 mmol, 1 equiv) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7), charged with TFE (**1a**, 3.5 atm, an excess amount) as a gas, and heated. Monitoring the reaction was performed by means of ^{19}F NMR spectroscopy. The yields of the monodefluoroborylated product **7a** were determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard.

Procedures for defluoroborylation of TFE (1a), trifluoroalkenes (1h-1j), and monofluoroalkenes (1e and 1f) (Table 4.2)

2-Trifluorovinyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (7a)



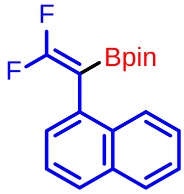
To a solution of (IPr)CuO^{t}Bu (2.6 mg, 0.005 mmol, 0.050 equiv) in THF/THF-d_8 (0.50 mL, v/v′ = 4/1) were added (Bpin)$_2$ (**10a**, 25.4 mg, 0.100 mmol, 1 equiv) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7), and then TFE (**6a**, 3.5 atm, an excess amount) was charged as a gas. The reaction mixture was heated at 100 °C for 20 h. Monitoring the reaction was performed by means of ^{19}F NMR spectroscopy. Formation of **7a** was confirmed by ^{19}F NMR and HRMS analyses, and the yield was determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard;

Yield (^{19}F NMR): 93% (0.093 mmol);

^{19}F NMR (THF-d_8) δ –204.3 (br d, J_{FF} = 114.7 Hz, 1F), –111.9 (dd, J_{FF} = 114.7, 42.4 Hz, 1F), –87.2 (dd, J_{FF} = 42.4, 22.6 Hz, 1F);

HRMS (EI) *m*/*z* 208.0883 (208.0882 calcd for $C_8H_{12}BF_3O_2^+$, [M]$^+$).

2-(2,2-Difluoro-1-(naphthalen-1-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (7h)



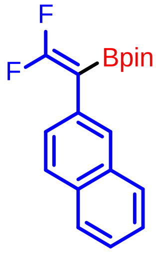
To a solution of (IPr)CuO^{t}Bu (2.6 mg, 0.005 µmol, 0.050 equiv) in THF/THF-d_8 (0.50 mL, v/v′ = 4/1) were added (Bpin)$_2$ (**10a**, 38.1 mg, 0.150 mmol, 1.5 equiv) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a J-Young tube, and then 1-(trifluorovinyl)naphthalene (**1h**, 20.8 mg, 0.100 mmol, 1 equiv) was added. The reaction mixture was heated at 100 °C for 20 h. Monitoring the reaction was performed by means of ^{19}F NMR spectroscopy. Formation of **7h** was confirmed by ^{19}F NMR and HRMS analyses, and the yield was determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard;

Yield (^{19}F NMR): 21% (0.021 mmol);

^{19}F NMR (THF-d_8) δ –74.4 (s, 1F), –69.8 (s, 1F);

HRMS (EI) *m*/*z* 316.1441 (316.1446 calcd for $C_{18}H_{19}BF_2O_2^+$, [M]$^+$).

2-(2,2-Difluoro-1-(naphthalen-2-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (7i)



To a solution of (IPr)CuO^{t}Bu (3.9 mg, 0.0074 µmol, 0.050 equiv) in THF/THF-d_8 (0.50 mL, v/v′ = 4/1) were added (Bpin)$_2$ (**10a**, 57.2 mg, 0.225 mmol, 1.5 equiv) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a J-Young tube, and then 2-(trifluorovinyl)naphthalene (**1i**, 31.2 mg, 0.150 mmol, 1 equiv) was added. The reaction mixture was heated at 100 °C for 20 h. Monitoring the reaction was performed by means of ^{19}F NMR spectroscopy. The yield of **7c** (75 µmol, 50%) was determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard. To the residue was added *n*-hexane (ca. 10 mL), and the resulting suspension was filtered through a Celite®. The filtrate was concentrated *in vacuo* and purified by preparative HPLC (CHCl$_3$) to give **7c** (20.0 mg, 0.063 mmol, 42%) as a colorless liquid;

^{1}H NMR (CDCl$_3$) δ 1.33 (s, 12H), 7.41–7.48 (m, 3H), 7.77 (br s, 1H), 7.80–7.82 (m, 3H);

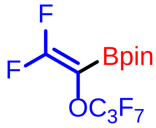
^{13}C NMR (CDCl$_3$) δ 24.8 (4C), 84.2 (2C), 125.9 (1C), 126.1 (1C), 127.7 (1C), 127.8 (1C), 127.8 (dd, $J_{C\text{–}F}$ = 2.6, 2.6 Hz, 1C), 128.0 (1C), 128.5 (dd, $J_{C\text{–}F}$ = 2.6, 2.6 Hz, 1C), 130.2 (dd, $J_{C\text{–}F}$ = 7.8, 1.2 Hz, 1C), 132.4 (1C), 133.4 (1C), 160.0 (dd, $J_{C\text{–}F}$ = 306.6, 298.3 Hz, 1C) (the signal for the carbon that is attached to the boron atom was not observed);

^{19}F NMR (CDCl$_3$) δ –70.7 (s, 1F), –68.8 (s, 1F);

^{11}B NMR (CDCl$_3$) δ 30.4;

HRMS (EI) *m/z* 316.1452 (316.1446 calcd for $C_{18}H_{19}BF_2O_2^+$, [M]$^+$).

2-(2,2-Difluoro-1-heptafluoropropyloxyvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (7j)



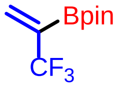
To a solution of a copper complex in THF/THF-d_8 (0.50 mL, v/v′ = 4/1) were added (Bpin)$_2$ (**10a**, 25.4 mg, 0.100 mmol, 1 equiv) and α,α,α-trifluorotoluene (12.2 μL, 0.100 mmol). The resultant solution was transferred into a J-Young tube, and then heptafluoropropyl trifluorovinyl ether (**1j**, 79.8 mg, 0.300 mmol, 3.0 equiv) was added. The reaction mixture was heated at 100 °C for 20 h. Monitoring the reaction was performed by means of ^{19}F NMR spectroscopy. Formation of **7j** was confirmed by ^{19}F NMR and HRMS analyses, and the yield was determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard. After determining the yield, the solvents were removed under reduced pressure and the residue was extracted with *n*-hexane (ca. 3 mL). The extract was passed through a pad of Celite® and washed with *n*-hexane (ca. 10 mL). The filtrate was concentrated under reduced pressure. To the residue was added CDCl$_3$ to obtain the ^{1}H and ^{19}F NMR spectra;

Yield (^{19}F NMR): 1% (1 μmol) using (IPr)CuO^{t}Bu (2.6 mg, 0.005 mmol, 0.050 equiv), 37% (0.037mol) using CuO^{t}Bu (0.68 mg, 0.005 mmol, 0.050 equiv) and xantphos (2.89 mg, 0.005 mmol, 0.050 equiv);

^{19}F NMR (CDCl$_3$) δ –129.3 (t, J_{FF} = 4.0 Hz, 2F), –88.3 (d, J_{FF} = 7.2 Hz, 1F), –85.6 (m, 2F), –81.4 (t, J_{FF} = 6.8 Hz, 3F), –71.3 (d m, J_{FF} = 7.2 Hz, 1F);

HRMS (EI) *m/z* 374.0743 (374.0736 calcd for $C_{11}H_{12}BF_9O_3^+$, [M]$^+$).

2-(3,3,3-Trifluoroprop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (9a)



To a solution of (IPr)CuO^{t}Bu (2.6 mg, 0.005 mmol, 0.050 equiv) in THF/THF-d_8 (0.50 mL, v/v′ = 4/1) were added (Bpin)$_2$ (**10a**, 25.4 mg, 0.100 mmol, 1 equiv) and α,α,α-trifluorotoluene (12.2 μL, 0.100 mmol). The resultant solution was transferred into a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7), and then 2,3,3,3-tetrafluoropropene (**1e**, HFO-1234yf, 3.5 atm, the excess amount) was charged as a gas.

The reaction mixture was heated at 100 °C for 20 h. Monitoring the reaction was performed by means of ^{19}F NMR spectroscopy. Formation of **7e** was confirmed by ^{19}F NMR and HRMS analyses, and the yield was determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard. After determining the yield, the solvents were removed under reduced pressure and the residue was extracted with *n*-hexane (ca. 3 mL). The extract was passed through a pad of Celite® and washed with *n*-hexane (ca. 10 mL). The filtrate was concentrated under reduced pressure. To the residue was added $CDCl_3$ to obtain the ^{1}H and ^{19}F NMR spectra;

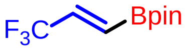
Yield (^{19}F NMR): 65% (0.065 mmol);

^{1}H NMR ($CDCl_3$) δ 1.29 (s, 12H), 6.32 (br s, 1H), 6.40 (br s, 1H);

^{19}F NMR ($CDCl_3$) δ –67.3 (d, J_{FH} = 2.7 Hz, 3F);

HRMS (EI) *m/z* 222.1043 (222.1039 calcd for $C_9H_{14}BF_3O_2^+$, $[M]^+$).

(*E*)-2-(3,3,3-Trifluoroprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (7f)



To a solution of CuO^{t}Bu (0.68 mg, 0.005 mmol, 0.050 equiv) and xantphos (2.89 mg, 0.005 mmol, 0.050 equiv) in THF/THF-d_8 (0.50 mL, v/v′ = 4/1) were added $(Bpin)_2$ (**10a**, 25.4 mg, 0.100 mmol, 1 equiv) and α,α,α-trifluorotoluene (12.2 μL, 0.100 mmol). The resultant solution was transferred into a J-Young tube, and then (*E*)-1,3,3,3-tetrafluoropropene (**1f**, HFO-1234ze, 3.5 atm, an excess amount) was charged as a gas. The reaction mixture was heated at 100 °C for 20 h. Monitoring the reaction was performed by means of ^{19}F NMR spectroscopy. Formation of **7f** was confirmed by ^{19}F NMR spectroscopy and HRMS analysis, and the yields were determined by ^{19}F NMR spectroscopy using α,α,α-trifluorotoluene as an internal standard. After determining the yield, the solvents were removed under reduced pressure and the residue was extracted with *n*-hexane (ca. 3 mL). The extract was passed through a pad of Celite® and washed with *n*-hexane (ca. 10 mL). The filtrate was concentrated under reduced pressure. To the residue was added $CDCl_3$ to obtain the ^{1}H and ^{19}F NMR spectra;

Yield (^{19}F NMR): 87% (0.087 mmol);

^{1}H NMR ($CDCl_3$) δ 1.28 (s, 12H), 6.25 (dq, J_{HH} = 18.1 Hz, J_{HF} = 1.8 Hz, 1H), 6.47 (dq, J_{HH} = 18.1 Hz, J_{HF} = 6.2 Hz, 1H);

^{19}F NMR ($CDCl_3$) δ –70.2 (dd, J_{FH} = 6.2, 1.8 Hz, 3F);
HRMS (EI) *m*/*z* 222.1038 (222.1039 calcd for $C_9H_{14}BF_3O_2^+$, $[M]^+$).

Stoichiometric reactions (Scheme 4.2)

Reaction of TFE (6a) with 10a in the presence of (IPr)CuO^{t}Bu (Scheme 4.2A)

To a solution of (IPr)CuO^{t}Bu (10.4 mg, 0.02 mmol, 1 equiv) in THF/THF-d_8 (0.50 mL, v/v′ = 4/1) were added $(Bpin)_2$ (**10a**, 5.1 mg, 0.02 mmol, 1.0 equiv) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7), and then TFE (**1a**, 3.5 atm, the excess amount) was charged as a gas. The reaction mixture was stirred at room temperature for 15 min. The yield of **9** was determined by ^{19}F NMR spectroscopy using α,α,α-trifluorotoluene as an internal standard. In the reaction mixture, the generation of FBpin was detected (^{19}F NMR: δ –154 ppm in THF-d_8) and this chemical shift was identical to that of the authentic sample (prepared from $Et_3N\cdot 3HF$ and HBpin).[S1]

Isolation of 9: A mixture of (IPr)CuO^{t}Bu (52.5 mg, 0.100 mmol, 1.0 equiv), $(Bpin)_2$ (**10a**, 25.4 mg, 0.100 mmol, 1 equiv) and 1,4-diazabicyclo[2.2.2]octane (DABCO) (11.2 mg, 0.100 mmol, 1.0 equiv) was dissolved in THF (5.0 mL). The resulting solution was transferred into an autoclave reactor, and then TFE (**1a**, 3.5 atm, an excess amount) was charged into the reactor. The reaction mixture was stirred at room temperature for 1 h. After purging the unreacted TFE from the reactor (***caution***: The reaction mixture must be handled in a well-ventilated fume hood.), the reaction mixture was concentrated *in vacuo*. The residue was washed with *n*-pentane (ca. 5 mL) several times to afford **9** as a white solid (45.2 mg, 0.085 mol, 85%). A single crystal suitable for X-ray diffraction analysis was prepared by recrystallization from THF/*n*-hexane at 22 °C.

DABCO was used as a FBpin scavenger. A gradual decomposition of **9** in the reaction mixture was observed when the reaction of (IPr)CuBpin with TFE was conducted in the absence of DABCO.

^{1}H NMR (THF-d_8) δ 1.23 (d, J_{HH}= 6.8 Hz, 12H), 1.30 (d, J_{HH} = 6.8 Hz, 12H), 2.63 (sept, J_{HH} = 6.8 Hz, 4H), 7.34 (d, J_{HH} = 7.7 Hz, 4H), 7.48 (d, J_{HH} = 7.7 Hz, 2H), 7.51 (s, 2H);
^{13}C NMR (THF-d_8) δ 23.8, 29.4, 124.4, 124.6, 130.9, 135.7, 146.4, 183.3 (the peaks assigned to CF_2=CF moiety were not distinctly observed due to their multiple coupling);

^{19}F NMR (THF-*d*$_8$) δ –195.2 (dd, J_{FF} = 32.8, 97.0 Hz, 1F), –138.2 (dd, J_{FF} = 97.0, 97.0 Hz, 1F), –102.3 (dd, J_{FF} = 32.8, 97.0 Hz, 1F);
Anal. calcd. for $C_{29}H_{36}CuF_3N_2$: C, 65.33; H, 6.81; N, 5.25. Found: C, 65.37; H, 7.20; N, 5.19.

Reaction of vinylcopper(I) 9 with 10a (Scheme 4.2B)

To a solution of **9** (10.6 mg, 0.02 mmol, 1 equiv) in THF/THF-*d*$_8$ (0.50 mL, v/v′ = 4/1) were added (Bpin)$_2$ (**10a**, 25.4 mg, 0.100 mmol, 5.0 equiv) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7), and then 2,3,3,3-tetrafluoropropene (**1e**, HFO-1234yf, 3.5 atm, an excess amount) was charged as a gas. The reaction mixture was heated at 100 °C for 1 h. Formation of **7a** was confirmed by ^{19}F NMR analysis and the yield (0.012 mmol, 60%) was determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard.

Copper-mediated arylation of 7a (Scheme 4.4)

To a solution of (IPr)CuO*ᵗ*Bu (2.6 mg, 0.005 mmol, 0.050 equiv) in THF/THF-*d*$_8$ (0.50 mL, v/v′ = 4/1) were added (Bpin)$_2$ (**10a**, 25.4 mg, 0.100 mmol, 1 equiv) and α,α,α-trifluorotoluene (12.2 µL, 0.100 mmol). The resultant solution was transferred into a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7), and then TFE (**1a**, 3.5 atm, an excess amount) was charged as a gas. The reaction mixture was stirred at 100 °C for 20 h. After replacement of TFE gas with N_2, to the mixture were added CuO*ᵗ*Bu (13.6 mg, 0.100 mmol, 1.0 equiv), 1,10-phen (18.0 mg, 0.100 mmol, 1.0 equiv), and 4-iodobenzotrifluoride (32.6 mg, 0.120 mmol, 1.2 equiv). The reaction mixture was heated at 60 °C for 3 h. Formation of 1-trifluoromethyl-4-(1,2,2-trifluorovinyl)benzene was confirmed by ^{19}F NMR and GCMS analyses, and the yield (0.057 mmol, 57% from **10a**) was determined by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard;
^{19}F NMR (THF-*d*$_8$) δ –180.3 (dd, J_{FF} = 109.2, 33.9 Hz, 1F), –117.3 (dd, J_{FF} = 109.2, 64.0 Hz, 1F), –103.1 (dd, J_{FF} = 64.0, 33.9 Hz, 1F), –65.5 (s, 3F);
MS (EI, *m*/*z* (%)): 226 (100) $[M]^+$, 202 (20), 176 (26), 157 (30).
The chemical shifts were consistent with those reported in the literature.[S2]

References for experimental section

S1 T. Braun, M. A. Salomon, K. Altenhöner, M. Teltewskoi, S. Hinze, *Angew. Chem., Int. Ed.* **2009**, *48*, 1818.

S2 M. Ohashi, T. Kambara, T. Hatanaka, H. Saijo, R. Doi, S. Ogoshi, *J. Am. Chem. Soc.* **2011**, *133*, 3256.

Conclusion

Described in this thesis were the studies on the C–F bond transformation reactions of ployfluoroalkenes via fluoroalkylcopper key intermediates. The studies enable efficient and straightforward transformations of ployfluoroalkenes into more valuable organofluorine compounds. Fluoroalkylcopper complexes generated by the 1,2-addition of organocopper species toward polyfluoroalkenes were found to play crucial roles in these transformation reactions.

In chapter 2, the copper-mediated one-pot synthesis of trifluorostyene derivatives was described. A variety of trifluorostyrene derivatives were prepared directly from tetrafluoroethylene and arlyboronates. 2-Aryl-1,1,2,2-tetrafluoroethylcopper complexes, which were generated by the carbocupration of TFE, underwent β-fluorine elimination by the treatment of a Lewis acid, leading to the trifluorostyrene derivatives. Furthermore, α-fluorine elimination of the fluoroalkylcopper complex was also achieved by using a Lewis acid, leading to the dimer of the resulting fluorocarbene species. Thus, the proper choice of Lewis acids enables the selective fluorine elimination of the fluoroalkyl copper complexes.

In chapters 3 and 4, the practical synthetic methods for either silylated or borylated fluoroalkenes via the copper-catalyzed defluorosilylation or defluoroborylation of polyfluoroalkenes were described. The resulting silylated and borylated compounds are expected to serve as useful synthetic intermediates that take advantage of reliable transformations based on versatile well-established organosilane and organoboron chemistries. Mechanistic studies, which were based on stoichiometric reactions of copper complexes, revealed the reaction pathways clearly.

These results enabled that the combination of polyfluoroalkenes and organocopper complexes would allow us to expand the utility of polyfluoroalkenes. Thus, the studies in this thesis will provide new strategies of the transformation of polyfluoroalkenes in organic synthesis and in fluorine chemical industry. In addition, I believe that these studies will give a significant development in the field of materials and pharmaceutical sciences.

List of Publications

1. Copper-Mediated One-Pot Synthesis of Trifluorostyrene Derivatives from Tetrafluoroethlene and Arylboronate
   Kotaro Kikushima, Hironobu Sakaguchi, Hiroki Saijo, Masato Ohashi, Sensuke Ogoshi
   Chem. Lett. **2015**, *44*, 1019–1021.
2. Fluorinated Vinylsilanes from the Copper-Catalyzed Defluorosilylation of Fluoroalkene Feedstocks
   Hironobu Sakaguchi, Masato Ohashi, Sensuke Ogoshi
   Angew. Chem. Int. Ed. **2017**, *Early View* (DOI: 10.1002/anie.201710866)
3. Copper-Catalyzed Regioselective Monodefluoroborylation of Polyfluoroalkenes En Route to Diverse Fluoroalkenes
   Hironobu Sakaguchi, Yuta Uetake, Masato Ohashi, Takashi Niwa, Sensuke Ogoshi, Takamitsu Hosoya
   J. Am. Chem. Soc. **2017**, *139*, 12855–12862.

Supplementary Publications

1. Base-Free Hiyama Coupling Reaction via a Group 10 Metal Fluoride Intermediate Generated by C–F Bond Activation
   Hiroki Saijo, Hironobu Sakaguchi, Masato Ohashi, Sensuke Ogoshi
   Organometallics **2014**, *33*, 3669–3672.
2. Pentacoordinated Carboxylate π-allyl-Allyl Nickel Complexes as Key Intermediates for Ni-catalyzed Direct Amination of Allylic Alcohols
   Yusuke Kita, Hironobu Sakaguchi, Yoichi Hoshimoto, Daisuke Nakauchi, Yasuhito Nakahara, Jean-François Carpentier, Sensuke Ogoshi, Kazushi Mashima
   Chem. Eur. J. **2015**, *21*, 14571–14587.