Doctoral Dissertation

Studies on Transformation of Tetrafluoroethylene by Using Palladium or Copper Complexes

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Preface and Acknowledgement

The study in this thesis has been carried out under the direction of Professor Sensuke Ogoshi at the Department of Applied Chemistry, Faculty of Engineering, Osaka University from April 2009 to March 2015. The thesis described the transformation of tetrafluoroethylene with palladium or copper complexes.

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Contents

Abbreviations

The following abbreviations are used in the thesis.

anal.	elemental analysis
Ac	acetyl
atm	atmospheric pressure
aq.	aqueous
Ar	aryl
br	broad
Bn	benzyl
Bu	butyl
cat.	catalyst
cf.	confer
CI	chemical ionization
cod	1,5-cyclooctadiene
Cy	cyclohexyl
Cyp	cyclopentyl
°C	degrees Celsius
calcd	calculated
d	doublet
δ	chemical shift of NMR signal in ppm
dba	dibenzylideneacetone
DCC	*N,N'*-dicyclohexylcarbodiimide
DMAP	*N,N*-dimethylaminopyridine
EI	electron ionization
equiv	equivalent
Et	ethyl
GC	gas chromatography
h	hour(s)
Hex	hexyl
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
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
TMS	trimethylsilyl

Chapter 1

General Introduction

1.1 Organofluorine compounds

Organofluorine compounds have attracted much attention due to their remarkable applications in pharmaceutical and materials science.[1] Thus, a great deal of effort has been directed toward the development of a synthetic method for the organofluorine compounds. One of the fundamental methods in the synthesis of organofluorine compounds is a fluorination that enables the introduction of one fluorine atom into an organic compounds, and a variety of efficient and selective fluorination reactions have been achieved with fluorination reagents or transition-metal catalysts.[2] In addition to fluorination, a number of methods for the introduction of CF_3 group, so-called trifluoromethylation, have been developed.[3] In pharmaceutical chemistry, a variety of physiologically active compounds were synthesized by using the fluorination and trifluoromethylation. On the other hand, multifluorinated compounds that are used in materials science have suffered from the lack of straightforward synthetic methods applicable to a variety of multifluorinated compounds. Thus, the development of synthetic method for the multifluorinated compounds bearing various functional groups has been highly demanded.

1.2 Tetrafluoroethylene

Tetrafluoroethylene (TFE), which is used in the production of polytetrafluoroethylene and other copolymers in the fluorine industry, is one of the ideal starting materials for the synthesis of fluorinated compounds because it is an economical and environmentally benign feedstock with a negligible global warming potential.[4] Nevertheless, the synthetic method to transform TFE into organofluorine compounds has not been developed as fully as expected. In particular, little is known about the straightforward transformation of TFE into the complex organofluorine compounds bearing with various functional groups.

In stark contrast to non-fluorinated alkenes, TFE and other highly-fluorinated alkenes are known to react readily with nucleophiles, such as fluoride ion, resulting in the formation of carbanion intermediate stabilized electron-withdrawing fluorine or fluoroalkyl group (Figure 1.1). The high reactivity of fluorinated alkenes toward addition reaction is also rationalized by the repulsive interaction between π electrons and the lone electron pairs on the fluorine atom bounded to sp^2-carbon atom. Nucleophilic attack on the carbon atom induces rehybridization from sp^2 to sp^3 state, with the relief of the repulsive interaction.

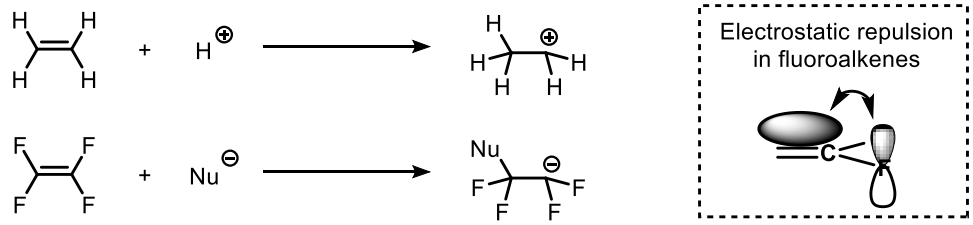
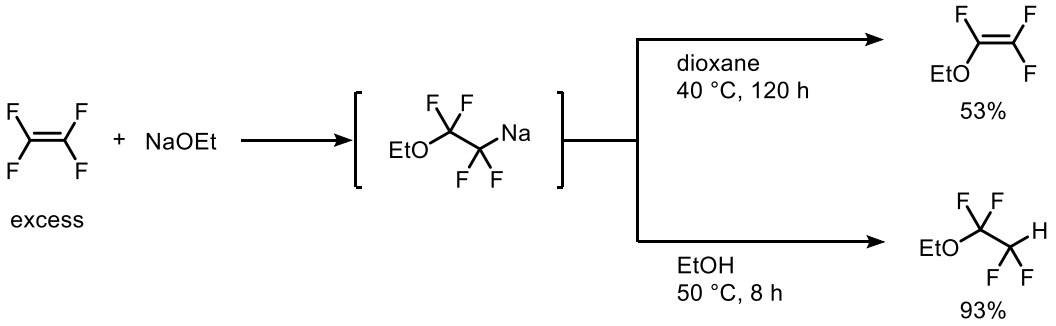


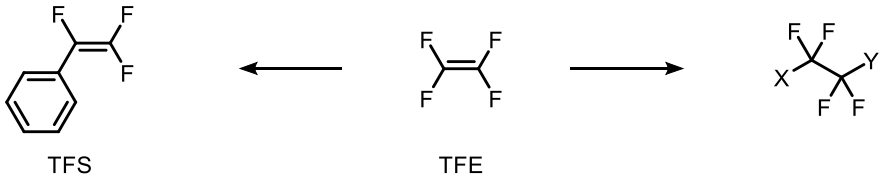
Figure 1.1. The model of inversely analogous reactivity of alkene and highly-fluorinated alkene.

The current synthetic methods for the transformation of TFE is mostly based on the addition reaction. For example, as shown in Scheme 1.1, TFE readily reacted with metal alkoxide to generate a substitution product ($ROCF{=}CF_2$) or an addition product ($ROCF_2CF_2H$).[5] The selectivity depends on the acidity of solvent and nucleophiles. The substitution product is obtained if the *β*-fluorine elimination occurs, and the addition product is obtained if the intermediate is immediately quenched by proton or a suitable electrophile. In fact, quite a few organofluorine compounds are produced from TFE through the addition reaction. However, the current synthetic methods based on the addition reaction generally have a serious limitation in the substrate scope. Therefore, it is highly demanded to developed an alternative synthetic method for the transformation of TFE into more valuable organofluorine compounds.



Scheme 1.1. Two pathways in addition reaction of TFE with NaOEt.[5b]

The purpose of this study is the development of the transition-metal catalyzed or mediated transformation reaction of TFE into useful organofluorine compounds, which are difficult to prepare by current synthetic methods. In particular, this study focus attention on *α*,*β*,*β*-trifluorostyrene (TFS) derivatives and compounds bearing tetrafluoroethylene-bridging structure (X–CF_2CF_2–Y) as the target compounds. The utility and current synthetic methods of these compounds are described in the following sections.



Scheme 1.2. Transformation of TFE into TFS or compounds bearing tetrafluoroethylene-bridging structure.

1.3 Trifluorostyrene

TFS derivatives are mainly used as a comonomer for the production of fluorinated polymers. Due to the ease of introduction of functional groups on the aromatic ring, TFS derivatives have been particularly utilized in functional polymers such as ion exchange membranes for fuel cell separators (Figure 1.2). [6]

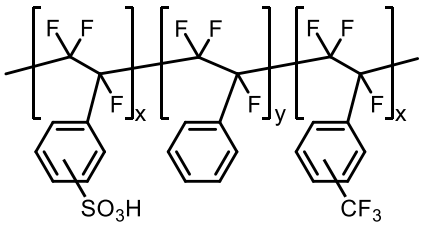
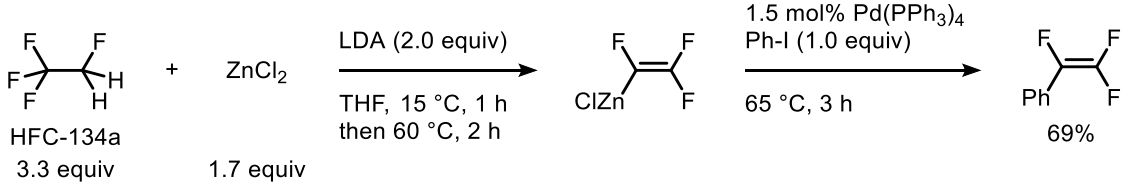


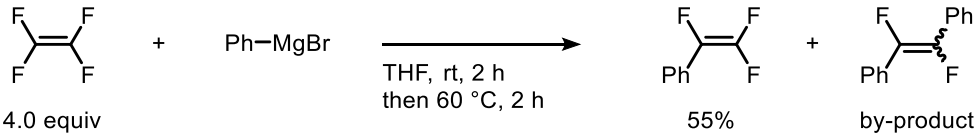
Figure 1.2. Example of membrane using TFS derivatives as monomers.

The most practical method for the synthesis of TFS derivatives would be the Pd(0)-catalyzed coupling reaction of iodoarenes with trifluorovinylzinc reagents prepared from 1,1,1,2-tetrafluoroethane (HFC-134a), as shown in Scheme 1.3.[7] However, HFC-134a has been subject to use restrictions due to its contribution to climate change (100 year GWP = 1430). Therefore, the development of an alternative synthetic method of TFS derivatives have been highly demanded.



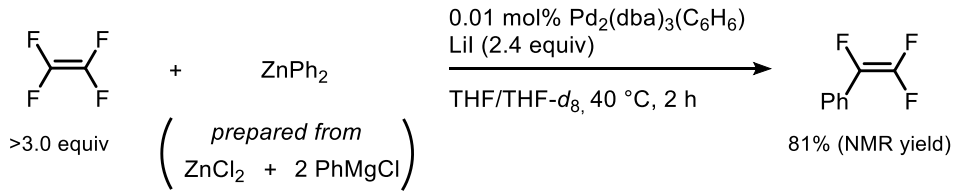
Scheme 1.3. Preparation of TFS from 1,1,1,2-tetrafluoroethane (HFC-134a).[7e]

Due to its low cost and environmental benign nature, TFE is an ideal starting material for the production of TFS derivatives. It has been known that the reaction of TFE with Grignard reagent gave TFS derivatives through the addition-elimination pathway.[8] However, the reaction suffered from low functional group tolerance caused from the use of Grignard reagent and the undesired formation of disubstituted product, 1,2-diaryl-1,2-difluoroethylene, resulted from the reaction of TFS with Grignard reagent. Due to these drawbacks, the reaction has been little used for the preparation of TFS derivatives.



Scheme 1.4. Reaction of tetrafluoroethylene with Grignard reagent.[9b]

An alternative route to TFS from TFE is Pd(0)-catalyzed coupling reaction through the C–F bond activation.[9] In 2011, our group reported the Pd(0)-catalyzed coupling reaction of TFE with organozinc reagents (Scheme 1.5).[10] In this reaction, the oxidative addition of a C–F bond of TFE is achieved by the addition of lithium iodide, with the formation of stable Li–F bond as driving force. TFE is transformed into TFS derivatives by using this reaction, however, there is still severe limitation about its functional group tolerance attributable to the nature of Grignard reagent.



Scheme 1.5. Reaction of tetrafluoroethylene with Grignard reagent.[10]

From the viewpoint of the functional group tolerance and the ease of handling, it is considered that the coupling reaction using organoboron compounds would be preferable to that using organozinc reagents.[11] Therefore, in order to develop the versatile transformation reaction of TFE into TFS, Pd(0)-catalyzed base-free coupling reaction of TFE with organoboron compounds has been developed in this study. The details and discussions are summarized in chapter 2. Furthermore, Pd(0)-catalyzed coupling reaction of TFE with organosilicon reagents are described in chapter 3.

1.4 Compounds bearing tetrafluoroethylene-bridging structure

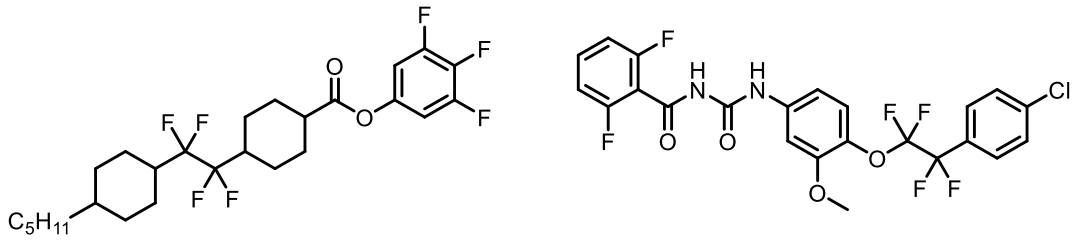
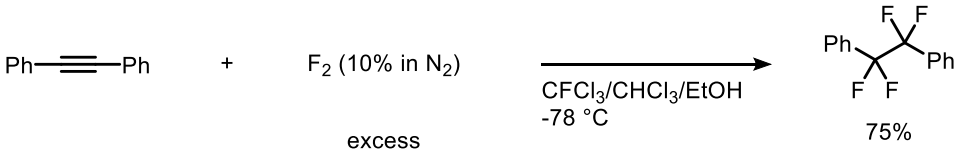


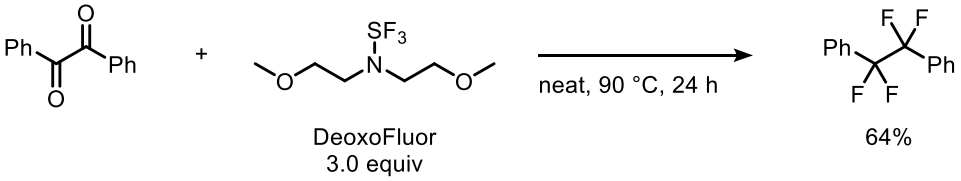
Figure 1.3. Selected examples for the application of compounds bearing tetrafluoroethyene-bridging structure. Left: a liquid-crystalline compound. Right: an insecticide.[12,13]

Compounds bearing tetrafluoroethylene-bridging structure (X–CF_2CF_2–Y) has found application in materials science and agrochemical research (Figure 1.3).[12,13] In particular, the structure has garnered a great deal of attention as a key structure in liquid-crystalline compounds because of its potential to influence the physical properties of these materials: clearing point, mesophase sequence, and rotational viscosity. Thus, materials containing the tetrafluoroethylene-bridging structure are expected to be used in the next generation of active-matrix liquid crystal displays with reduced power consumption.[12]

Tetrafluoroethylene-bridging structure are constructed via the fluorination of a carbon-carbon triple bond with F_2 or the deoxofluorination of 1,2-diketones with fluorination reagents such as DeoxoFluor.[14,15] However, these methods have low functional group tolerance and use toxic or costly reagent. Thus, the development of an alternative method without these reagents has been in high demand.

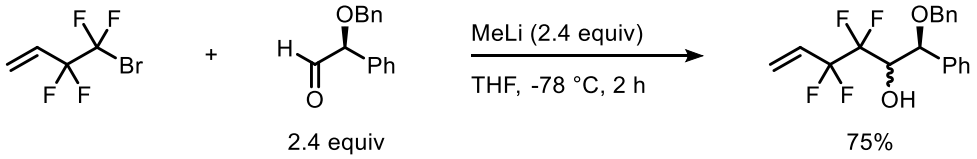


Scheme 1.5. Direct fluorination of alkynes by fluorine gas.[14]

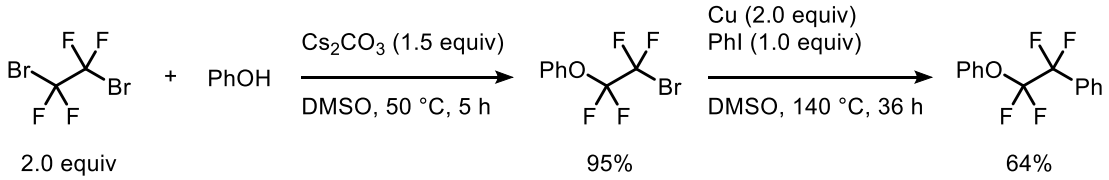


Scheme 1.6. Deoxofluorination of 1,2-diketones with DeoxoFluor.[15]

Another synthetic method is the transformation of commercially-available starting materials bearing tetrafluoroethylene-bridging structure. For example, Konno developed the transformation reactions of 4-bromo-3,3,4,4-tetrafluoro-1-butene (Scheme 1.7).[16] Hu reported Cu(I)-mediated synthesis of 1-aryloxy-2-phenyl-1,1,2,2-tetrafluoroethanes from 1-aryloxy-2-bromo-1,1,2,2-tetrafluoroethanes, which was prepared from commercially-available 1,2-dibromo-1,1,2,2-tetrafluoroethane (Scheme 1.8).[17] However, the structure of compounds that are obtained by these reactions is quite limited. In addition, the starting materials in these reactions, 4-bromo-3,3,4,4-tetrafluoro-1-butene and 1,2-dibromo-1,1,2,2-tetrafluoroethane, are produced from TFE.[18] Therefore, it is highly desired to develop the versatile and straightforward transformation reaction from TFE to compounds bearing tetrafluoroethylene-bridging structure.



Scheme 1.7. Transformation of 4-bromo-3,3,4,4-tetrafluoro-1-butene.[16]



Scheme 1.8. Transformation of 1,2-dibromo-1,1,2,2-tetrafluoroethane. [17]

In this study, in order to achieve the efficient, versatile, and straightforward transformation of TFE into compounds bearing tetrafluoroethylene-bridging structure, a novel Cu(I)-mediated carbocupration of TFE to form 2-aryl-1,1,2,2-tetrafluoroethyl copper complex was developed. Its synthesis, characterization with X-ray diffraction analysis and NMR analysis, and the synthetic utilities of the complex were described in chapter 4.

1.5 References and notes

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Chapter 2

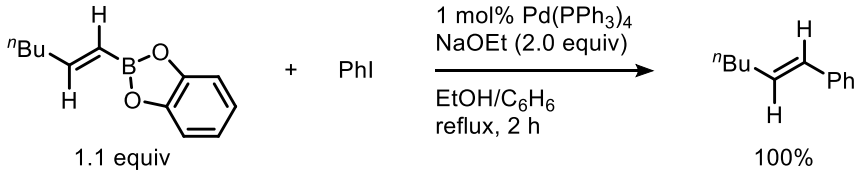
Pd(0)-Catalyzed Base-Free Suzuki-Miyaura Coupling of TFE

Abstract

In the presence of catalytic amount of Pd(0) and P^iPr_3, the coupling reaction of TFE with organoboronates took place without the addition of base to afford the TFS derivatives in good yields. This is the first base-free Suzuki-Miyaura coupling reaction. A fluoropalladium(II) key intermediate generated by the oxidative addition of a C–F bond of TFE was isolated and its structure was clearly determined by X-ray diffraction analysis. Mechanistic study indicated that the fluoropalladium complex is reactive enough toward non-activated organoboronate, which enables the catalytic reaction to proceed without base. This study also disclosed that the base-free system is applicable to the coupling reaction using other fluoroalkenes and fluoroarenes.

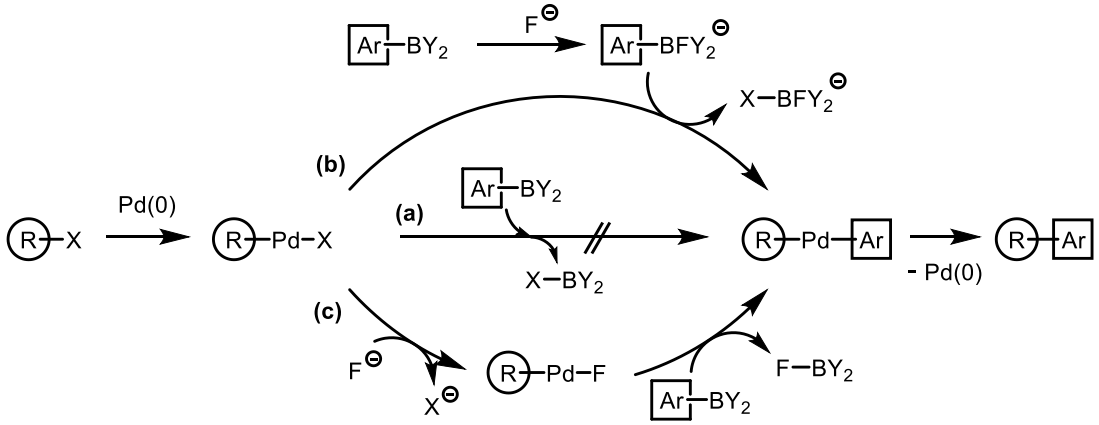
2.1 Introduction

Since the seminal work by Suzuki in 1979, Pd(0)-catalyzed coupling reaction of aryl halides with organoboron compounds, which is called Suzuki-Miyaura coupling, has been widely used to construct new C–C bond.[19] Organoboron compounds are low-cost, easy to handle, and have a broad functional group tolerance, which makes the method suitable for practical use both in academic and industrial chemistry. However, the Suzuki-Miyaura coupling requires a base such as hydroxide, carbonate, or fluoride in order to activate organoboron reagent or palladium intermediate. Until this study, to the best of our knowledge, base-free Suzuki-Miyaura coupling has never been reported.[20]



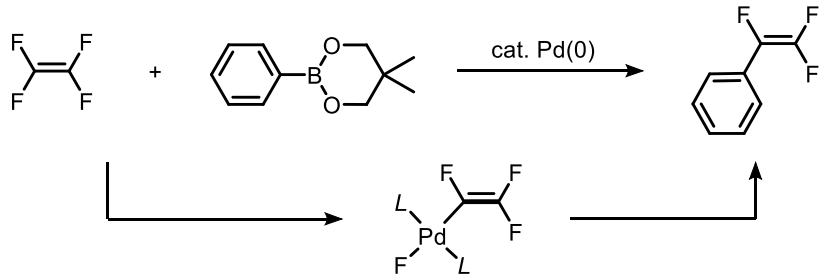
Scheme 2.1. Seminal work for the Suzuki-Miyaura coupling.[19a]

Due to the weak reactivity of organoboron compounds, transmetalation of palladium(II) halide with organoboron compound, which is a key step in the Suzuki-Miyaura coupling, is known not to occur without base (Scheme 2.2, path a).[21] Although it would be difficult to reveal completely the activation mechanism by base, it has been considered that there would be two distinct pathways in the transmetalation step. One plausible pathway is through the reactive borate generated from the reaction of organoboron compounds with base (path b). The other is through the reactive palladium intermediate, such as alkoxypalladium and fluoropalladium, generate from palladium intermediate with base (path c). In recent studies, it is suggested that the latter pathway would be more plausible in the catalytic reaction.[22]



Scheme 2.2. Mechanisms of transmetalation with organoboron compounds. (a) direct (not proceed). (b) via the activation of organoboron compound. (c) via the activation of palladium complex.

Described in this chapter is a base-free Suzuki-Miyaura coupling of TFE with organoboronates. In the reaction, a fluoropalladium(II) intermediate generated by the oxidative addition of a C–F bond of TFE is found to be reactive enough toward organoboronates, which enables the catalytic reaction to proceed without base.

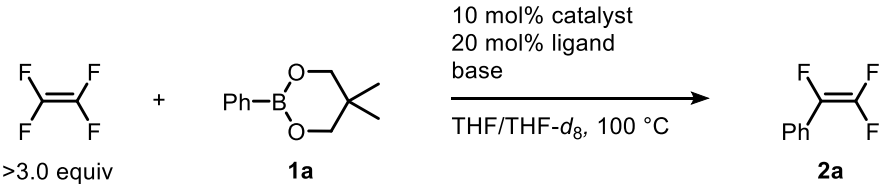


Scheme 2.3. Pd(0)-catalyzed base-free Suzuki-Miyaura coupling of TFE with organoboronates.

2.2 Development of the catalytic reaction

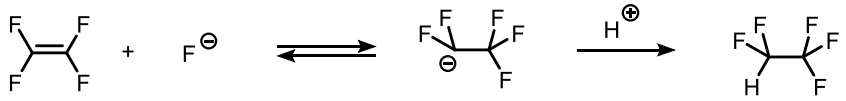
The results of the optimization of reaction conditions are summarized in Table 2.1. The coupling reaction of TFE with 5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane **1a** in the presence of the catalytic amount of $Ni(cod)_2/PCy_3$ gave trifluorostyrene **2a** in only 5% (entry 1). On the other hand, by using $Pd(dba)_2$ catalyst and PCy_3 ligand, the coupling reaction of TFE with **1a** proceeded at 100 °C without any base to afford **2a** in 66% yield (entry 2). No reaction occurred when using PPh_3 (entry 3). As a result of ligand screening, P^iPr_3 was found to be the best ligand to give **2a** in 87% yield (entry 5). In addition, survey on the effect of the base on the reaction showed that the addition of base diminished the yield of **2a** dramatically (entries 6 and 7). In the case using fluoride anion as the base, the addition reaction of fluoride anion with TFE occurred to generate pentafluoroethane (Scheme 2.4). Based on these results, the conditions as described in entry 5 were set as the optimized reaction conditions.

Table 2.1. Optimization of the reaction conditions.



entry	catalyst	ligand	base	time	yield
1	$Ni(cod)_2$	PCy_3	none	20 h	5%
2	$Pd(dba)_2$	PCy_3	none	5 h	66%
3	$Pd(dba)_2$	PPh_3	none	20 h	0%
4	$Pd(dba)_2$	P^nBu_3	none	5 h	44%
5	$Pd(dba)_2$	P^iPr_3	none	7 h	87%
6	$Pd(dba)_2$	P^iPr_3	1.2 equiv K_2CO_3	7 h	10%
7	$Pd(dba)_2$	P^iPr_3	1.2 equiv CsF	20 h	0%

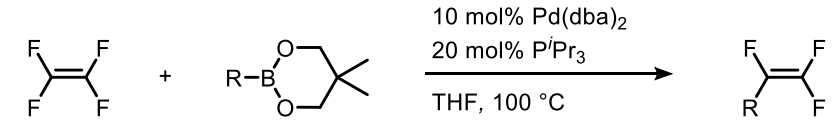
Yields were determined by ^{19}F NMR.

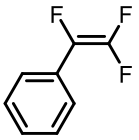
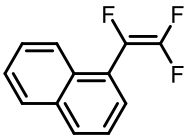
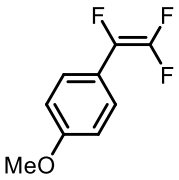
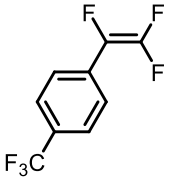
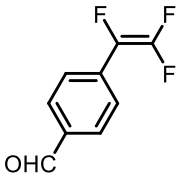
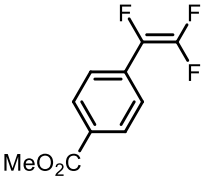
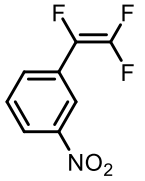
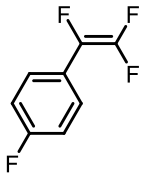
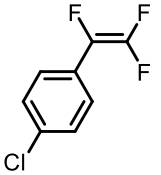
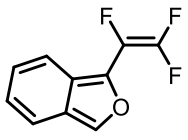
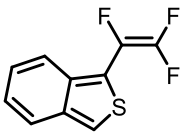
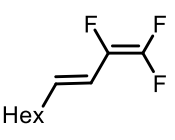


Scheme 2.4. Addition reaction of TFE with fluoride ion.

With the optimized reaction conditions, the scope of the Pd(0)-catalyzed base-free Suzuki-Miyaura coupling of TFE was investigated with respect to the arylboronates **1**. As shown in Table 2.2, TFS derivatives **2** with various kinds of functional group were synthesized by this reaction. Both the electron-rich and electron-deficient organoboronates were efficiently converted into the corresponding TFS derivatives (**2c** and **2d**). Functional groups such as formyl, methoxycarbonyl, and nitro group were tolerated through the reaction (**2e-g**). In addition, arylboronates bearing C–F or C–Cl bond, heteroaromatic organoboronates, and an alkenylboronate were applicable in the reaction, affording the corresponding products in good yields (**2h-l**).

Table 2.2. Substrate scope of base-free Suzuki-Miyaura coupling of TFE.

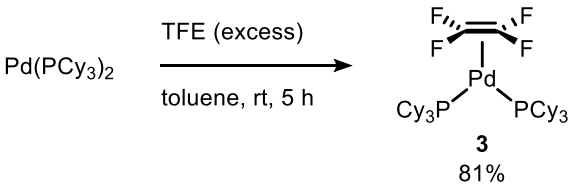


 **2a**, 20 h, 41% (87%)	 **2b**, 20 h, 65% (88%)	 **2c**, 20 h, 55% (82%)	 **2d**, 10 h, 31% (81%)
 **2e**, 10 h, 26% (63%)	 **2f**, 10 h, 41% (75%)	 **2g**, 10 h, 72% (86%)	 **2h**, 20 h, 43% (76%)
 **2i**, 10 h, 23% (74%)	 **2j**, 0.5 h, 61% (56%)	 **2k**, 0.5 h, 30% (58%)	 **2l**, (0.5 h, 73%)

Isolated yields. Values in parentheses are NMR yields determined by ^{19}F NMR.

2.3 Mechanistic study

To gain insight into the reaction mechanism, some stoichiometric reaction using palladium complexes were conducted. First, (η^2-TFE)Pd(PCy_3)$_2$ (**3**) was prepared by the reaction of Pd(PCy_3)$_2$ with TFE (Scheme 2.5). The structure of **3** was confirmed by X-ray diffraction analysis (Figure 2.1).



Scheme 2.5. Synthesis of complex **3**.

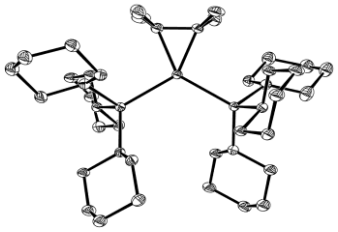
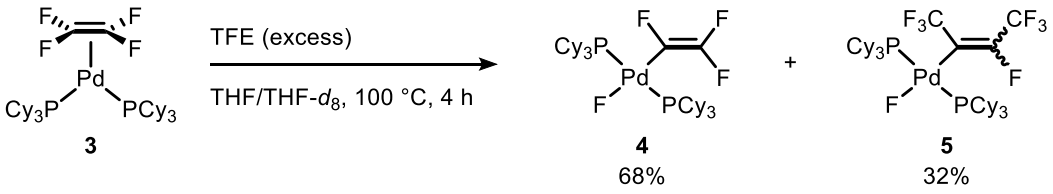


Figure 2.1. ORTEP structure of **3**. H atoms were omitted for clarity.

By heating of **3** at 100 °C with excess amount of TFE, the oxidative addition of a C–F bond of TFE proceeded to generate *trans*-(PCy_3)$_2$Pd(F)(CF=CF_2) (**4**) and *trans*-(PCy_3)$_2$Pd(F)(C(CF_3)F=CF_3) (**5**) in 68% and 32% yield, respectively. The formation mechanism of **5** was not revealed, but it was confirmed that no further reaction of TFE with **4** occurred under the reaction conditions.



Scheme 2.6. Oxidative addition of a C–F bond of TFE by heating of **3**.

The molecular structure of **4** was confirmed by X-ray diffraction analysis (Figure 2.2). In ^{19}F NMR analysis, in addition to three signals attributable to trifluorovinyl group (δ –99.9, –130.8, –149.7 in THF-d_8), a broad signal attributable to fluoride atom bound to palladium was observed in characteristic upfield (δ –317.9), which is consistent with the data of known fluoropalladium complexes.

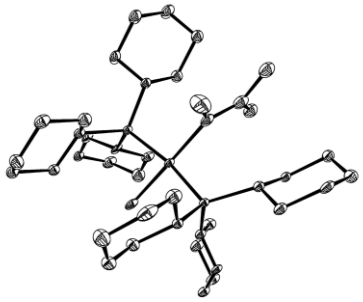
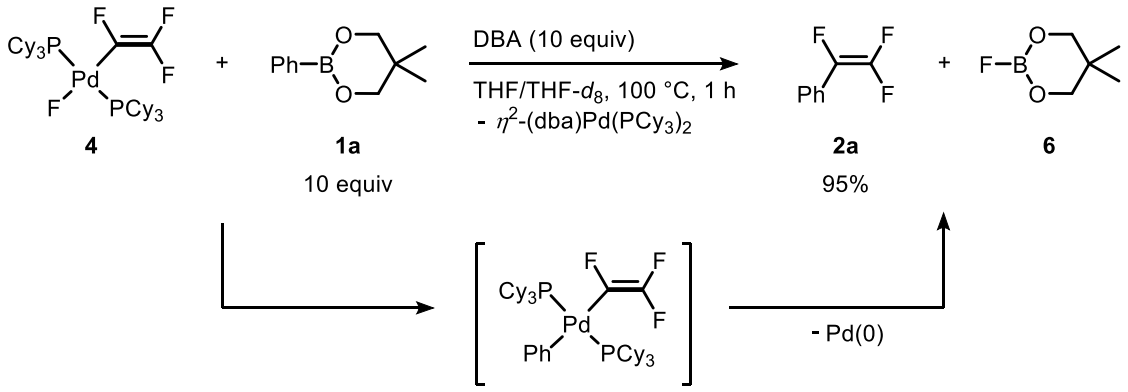


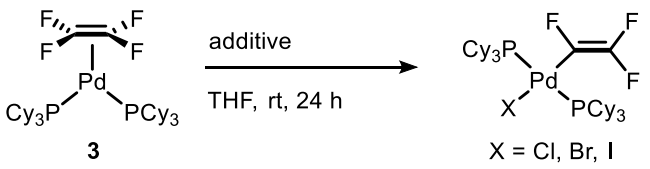
Figure 2.2. ORTEP structure of **4**. H atoms were omitted for clarity.

Next, the reactivity of **4** toward organoboronate was investigated. In the presence of DBA, the reaction of **4** with 10 equiv of **1a** in THF at 100 °C proceeded smoothly to afford **2a** in 95% yield (Scheme 2.7). The concomitant formations of **6** and (η^2-dba)Pd(PCy_3)$_2$ were observed by NMR analysis. Although it has been considered that the transmetalation of halopalladium complex with organoboron compound requires base, the reaction of **4** with **1a** occurred without any base. It is estimated that the formation of stable B–F bond would be driving force in the reaction.



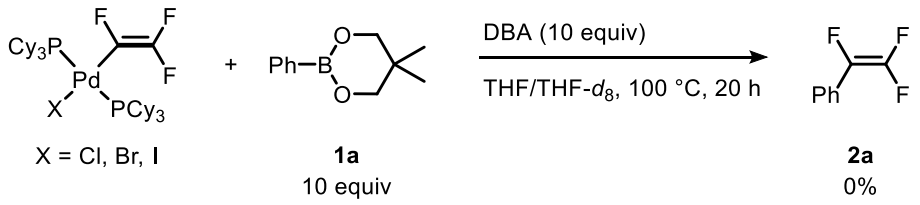
Scheme 2.7. Reaction of **4** with **1a** in the absence of base.

In stark contrast to fluoropalladium complex **4**, the corresponding halopalladium complexes *trans*-(PCy_3)$_2$Pd(X)(CF=CF_2) (X = Cl Br, I), which were prepared by the reaction shown in Scheme 2.8, did not react with **1a** under the same reaction conditions (Scheme 2.9). These results clearly indicated that the fluorine atom bounded to palladium has a crucial role in the transmetalation with organoboron compounds.



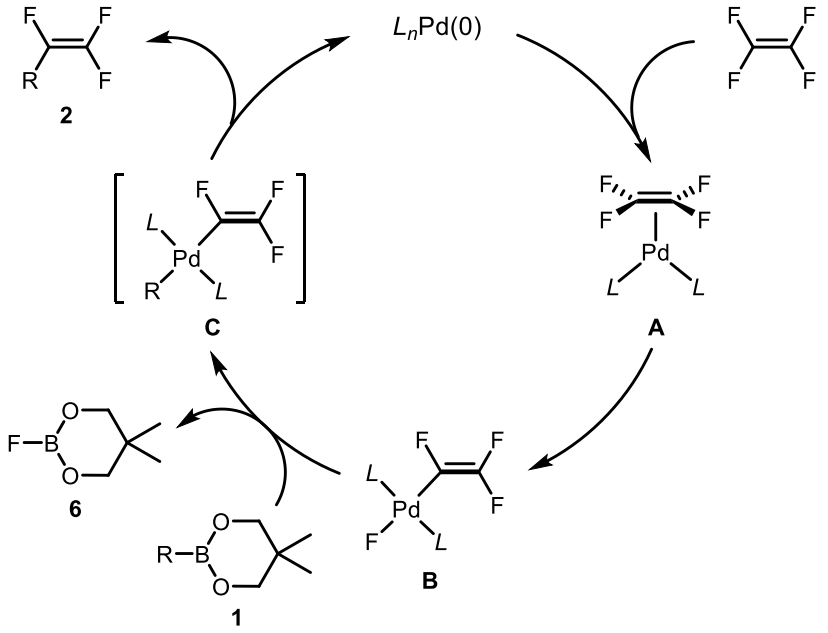
additive	X	yield
LiCl	Cl	96%
$MgBr_2$	Br	93%
LiI	I	87%

Scheme 2.8. Synthesis of *trans*-(PCy_3)$_2$Pd(X)(CF=CF_2) (X = Cl, Br, I).



Scheme 2.9. Reaction of *trans*-(PCy_3)$_2$Pd(X)(CF=CF_2) (X = Cl, Br, I) with **1a**.

On the basis of the results described above, it is estimated that the Pd(0)-catalyzed base-free coupling reaction of TFE with **1** would proceed as shown in Scheme 2.10. First, coordination of TFE to Pd(0) takes place to generate η^2-TFE complex **A**. Then, the oxidative addition of a C–F bond occurs to form trifluorovinylpalladium(II) fluoride intermediate **B**, which would be reactive enough to neutral organoboronate **1**. Transmetalation of **B** with **1** proceeds without base to afford **C**. Finally, reductive elimination gives the coupling product **2** with the regeneration of Pd(0) species.

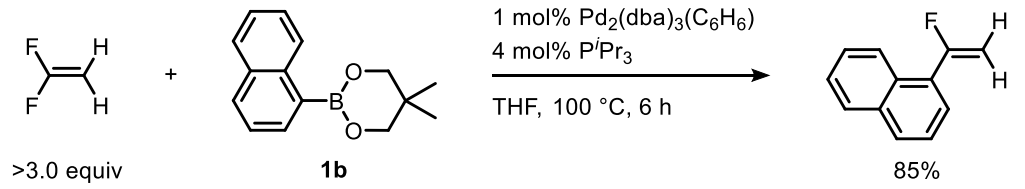


Scheme 2.10. A plausible reaction mechanism.

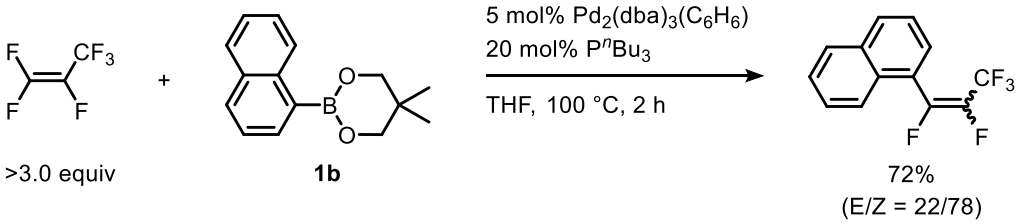
2.4 Application to other fluoroalkenes and fluoroarenes

As described above, the base-free Suzuki-Miyaura coupling of TFE was found to proceed through the fluoropalladium(II) intermediate generated by the oxidative addition of a C–F bond. This insight clearly indicated that the base-free strategy would be applicable to the reaction with other fluoroalkenes and fluoroarenes.[23]

In fact, in the presence of 1 mol% of $Pd_2(dba)_3(C_6H_6)$ and 4 mol% of P^iPr_3, the coupling reaction of 1,1-difluoroethylene proceeded at 100 °C without base, affording the 1-(1-fluorovinyl)naphthalene in 85% yield (Scheme 2.11). The reaction of hexafluoropropene using P^nBu_3 ligand gave the corresponding coupling product in 72% yield, as a cis/trans mixture (Scheme 2.12).



Scheme 2.11. Pd(0)-catalyzed base-free Suzuki-Miyaura coupling of 1,1-difluoroethylene.



Scheme 2.12. Pd(0)-catalyzed base-free Suzuki-Miyaura coupling of hexafluoropropene.

In addition, the base-free system was found to be applicable to fluoroarenes. In this case, the use of Ni(0) catalyst and a *N*-hetero cyclic carbene ($^{i}Pr_2Im$) ligand was effective. Radius reported that the oxidative addition of C–F bond on aromatic ring took place efficiently with Ni(0) and $^{i}Pr_2Im$ ligand to generate the corresponding fluoronickel(II) complexes.[24]

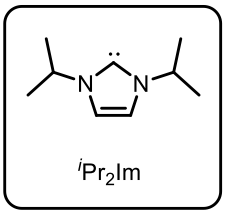
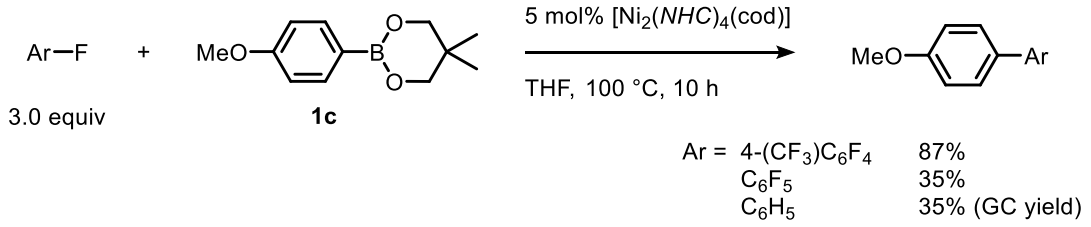


Figure 2.3. Structure of $^{i}Pr_2Im$.

In the presence of 5 mol% of $[Ni(^{i}Pr_2Im)_2]_2(cod)$, the coupling reaction of octafluorotoluene with **1c** proceeded smoothly without base to give the corresponding biaryl **8c** in 87% yield (Scheme 2.13). Under the same reaction conditions, the reaction with hexafluorobenzene also took place gave the coupling product in 35% yield. Furthermore, fluorobenzene was found to be applicable to the base-free coupling reaction.



Scheme 2.13. Ni(0)-catalyzed base-free Suzuki-Miyaura coupling of fluoroarenes.

2.5 Conclusion

In chapter 2, a Pd(0)-catalyzed base-free Suzuki-Miyaura coupling reaction of TFE was described. A variety of trifluorostyrene derivatives were synthesized in good yields. Notably, this is the first example of the Suzuki-Miyaura coupling reaction without base. Mechanistic study indicated that the fluoropalladium(II) key intermediate generated by the oxidative addition of a C–F bond would be reactive enough toward non-activated organoboron compounds, which enables the base-free coupling reaction. Furthermore, the base-free system was found to be applicable to other fluoroalkenes and fluoroarenes.

2.6 Experimental section

General remarks compatible to all the experimental part in this thesis

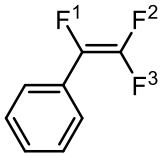
All manipulations were conducted under a nitrogen atmosphere using standard Schlenk or dry box techniques. ^{1}H, ^{11}B, ^{13}C, ^{19}F, and ^{31}P nuclear magnetic resonance spectra were recorded on Bruker AVANCE III 400 spectrometers at 25 °C unless otherwise stated. The chemical shifts in ^{1}H nuclear magnetic resonance spectra were recorded relative to Me_4Si or residual protonated solvent (C_6D_5H (δ 7.16), THF-d_7 (δ 1.73), $CDHCl_2$ (δ 5.32) or $CHCl_3$ (δ 7.26)). The chemical shifts in ^{11}B nuclear magnetic resonance spectra were recorded to BF_3 as an external standard. The chemical shifts in the ^{13}C spectra were recorded relative to Me_4Si or deutrated solvent (C_6D_6 (δ 128.1), THF-d_8 (δ 25.3), CD_2Cl_2 (δ 53.8) or $CDCl_3$ (δ 77.2)). The chemical shifts in ^{19}F nuclear magnetic resonance spectra were recorded to $CFCl_3$ as an external standard. The chemical shifts in ^{31}P nuclear magnetic resonance spectra were recorded to H_3PO_4 as an external standard. Medium-pressure column chromatography was carried out on a Biotage Flash Purification System Isolera, equipped with a 254 nm UV detector. Analytical gas chromatography (GC) was carried out on a Shimadzu GC-2014 gas chromatograph, equipped with a flame ionization detector. High resolution mass *spectrometry* (HRMS) and elementary analyses were performed at Instrumental Analysis Center, Faculty of Engineering, Osaka University. X-ray crystal data were collected by a Rigaku RAXIS-RAPID Imaging Plate diffractometer.

Materials: All commercially available reagents and solvents were used as received unless otherwise noted. THF, THF-d_8, and C_6D_6 were distilled from benzophenone ketyl prior to use. CD_2Cl_2 was distilled over CaH_2 prior to use.
Caution: Tetrafluoroethylene (TFE) is suspected to be carcinogens. The reaction mixture must be handled in a well-ventilated fume hood.

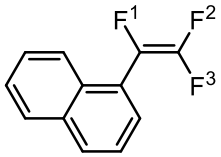
General procedure for the preparation of organoboronate (1): The preparation of **1** was conducted under air. To a solution of 2,2-dimethyl-1,3-propandiol (1.1 equiv) in toluene, boronic acid was added. The mixture was heated under reflux overnight. After cooling, water was added, and the product was extracted with $CHCl_3$ three times. The combined organic layer was washed with brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent under reduced pressure afforded **1** with sufficient purity.

General procedure for the optimization of the reaction conditions (Table 1.1): The reaction was conducted with a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7). A mixture of 5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane (**1a**: 19.0 mg, 0.10 mmol), catalyst, ligand, and base was dissolved in 0.50 mL of THF/THF-d_8 (v/v' = 4/1). The resulting solution was transferred into the tube, and then TFE (3.5 atm, >0.30 mmol) was charged. The reaction mixture was heated at 100 ºC until the reaction was terminated. Monitoring the reaction was performed by means of ^{19}F NMR spectroscopy. Yield was determined by ^{19}F NMR with $PhCF_3$ as an internal standard.

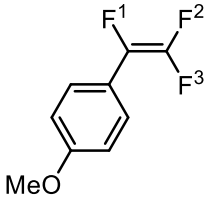
General procedure for the isolation of trifluorostyrenes (2): The reactions were conducted with an autoclave reactor. A mixture of **1** (1.0 mmol), $Pd(dba)_2$ (56.0 mg, 0.10 mmol) and P^iPr_3 (32.0 mg, 0.20 mmol) was dissolved in 10.0 mL of THF. The resulting solution was transferred into the autoclave reactor, and then TFE (3.5 atm) was charged. The reaction mixture was heated at 100 ºC for the given time. After the unreacted TFE was purged from the reactor, the reaction mixture was concentrated under reduced pressure. 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 under reduced pressure and purified by preparative HPLC ($CHCl_3$). The desired compounds were isolated as a $CHCl_3$ solution because of their high vapor pressure, and their yields were determined by means of ^{19}F NMR spectroscopy.



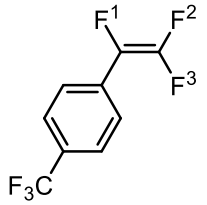
***α,β,β*-Trifluorostyrene (2a)**: Following the general procedure, the reaction with 5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane (**1a**) was conducted for 20 h to give **2a** (0.41 mmol, 41%). ^{19}F NMR (376 MHz, THF/THF-d_8, rt, δ/ppm): –179.0 (dd, J_{FF} = 32.7, 110.3 Hz, 1F, F^1), –118.5 (dd, J_{FF} = 73.5, 110.3 Hz, 1F, F^3), –104.2 (dd, J_{FF} = 32.7, 73.5 Hz, 1F, F^2).



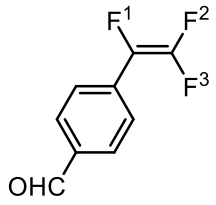
1-(1,2,2-Trifluorovinyl)naphthalene (2b): Following the general procedure, the reaction with 5,5-dimethyl-2-(1-naphthyl)-1,3,2-dioxaborinane (**1b**) was conducted for 20 h to give **2b** (0.65 mmol, 65%). ^{19}F NMR (376 MHz, THF/THF-d_8, rt, δ/ppm): –162.6 (dd, J_{FF} = 30.3, 118.1 Hz, 1F, F^1), –119.8 (dd, J_{FF} = 75.0, 118.1 Hz, 1F, F^3), –104.1 (dd, J_{FF} = 30.3, 75.0 Hz, 1F, F^2).



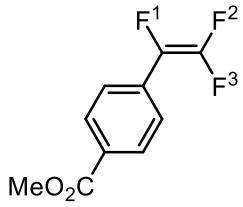
1-Methoxy-4-(1,2,2-trifluorovinyl)benzene (2c): Following the general procedure, the reaction with 5,5-dimethyl-2-(4-methoxyphenyl)-1,3,2-dioxaborinane (**1c**) was conducted for 20 h to give **2c** (0.55 mmol, 55%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 3.84 (s, 3H), 7.01 (d, J = 9.1 Hz, 2H), 7.43 (d, J = 9.1 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 55.4, 114.3, 119.7, 126.3, 128.9, 153.6, 160.1. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –178.1 (dd, J_{FF} = 31.2, 110.3 Hz, 1F, F^1), –119.9 (dd, J_{FF} = 79.1, 110.3 Hz, 1F, F^3), –104.9 (dd, J_{FF} = 31.2, 79.1 Hz, 1F, F^2).



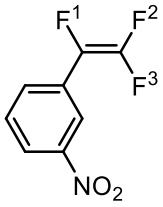
1-Trifluoromethyl-4-(1,2,2-trifluorovinyl)benzene (2d): Following the general procedure, the reaction with 2-(4-trifluoromethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**1d**) was conducted for 10 h to give **2d** (0.31 mmol, 31%). ^{19}F NMR (376 MHz, THF/THF-d_8, rt, δ/ppm): –179.8 (dd, J_{FF} = 32.7, 109.2 Hz, 1F, F^1), –115.0 (dd, J_{FF} = 65.3, 109.2 Hz, 1F, F^3), –100.8 (dd, J_{FF} = 32.7, 65.3 Hz, 1F, F^2).



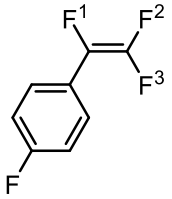
4-(1,2,2-Trifluorovinyl)benzaldehyde (2e): Following the general procedure, the reaction with 2-(4-formylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**1e**) was conducted for 10 h to give **2e** (0.26 mmol, 26%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.60 (d, J = 8.4 Hz, 2H), 7.93 (d, J = 8.4 Hz, 2H), 10.1 (s, 1H). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 124.7, 128.2, 130.1, 133.1, 136.2, 154.4, 191.4. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –180.1 (dd, J_{FF} = 32.6, 108.7 Hz, 1F, F^1), –112.7 (dd, J_{FF} = 63.3, 108.7 Hz, 1F, F^3), –97.9 (dd, J_{FF} = 32.6, 63.3 Hz, 1F, F^2).



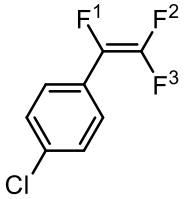
Methyl 4-(1,2,2-trifluorovinyl)benzoate (2f): Following the general procedure, the reaction with methyl 4-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)benzoate (**1f**) was conducted for 10 h to give **2f** (0.41 mmol, 41%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 3.91 (s, 3H), 7.50 (d, J = 8.6 Hz, 2H), 8.12 (d, J = 8.6 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 52.4, 124.1, 128.3, 130.0, 133.3, 131.6, 154.3, 166.4. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –180.2 (dd, J_{FF} = 32.7, 108.6 Hz, 1F, F^1), –113.8 (dd, J_{FF} = 65.4, 108.6 Hz, 1F, F^3), –99.2 (dd, J_{FF} = 32.7, 65.4 Hz, 1F, F^2).



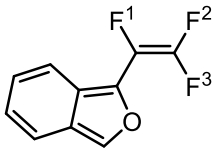
1-Nitro-3-(1,2,2-trifluorovinyl)benzene (2g): Following the general procedure, the reaction with methyl 5,5-dimethyl-2-(3-nitrophenyl)-1,3,2-dioxaborinane (**1g**) was conducted for 10 h to give **2g** (0.72 mmol, 72%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.61-8.34 (m, 4H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 119.4, 123.6, 127.5, 129.2, 129.9, 130.1, 148.7, 154.2. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –180.0 (dd, J_{FF} = 33.5, 109.8 Hz, 1F, F^1), –113.6 (dd, J_{FF} = 66.1, 109.8 Hz, 1F, F^3), –98.4 (dd, J_{FF} = 33.5, 66.1 Hz, 1F, F^2).



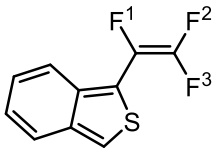
1-Fluoro-4-(1,2,2-trifluorovinyl)benzene (2h): Following the general procedure, the reaction with methyl 5,5-dimethyl-4-(fluorophenyl)-1,3,2-dioxaborinane (**1h**) was conducted for 20 h to give **2h** (0.43 mmol, 43%). ^{19}F NMR (376 MHz, THF/THF-d_8, rt, δ/ppm): –178.1 (dd, J_{FF} = 32.8, 110.3 Hz, 1F, F^1), –119.1 (dd, J_{FF} = 74.9, 110.3 Hz, 1F, F^3), –114.3 (m, 1F), –104.6 (dd, J_{FF} = 32.8, 74.9 Hz, 1F, F^2).



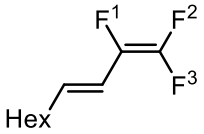
1-Chloro-4-(1,2,2-trifluorovinyl)benzene (2i): Following the general procedure, the reaction with 2-(4-chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**1i**) was conducted for 10 h to give **2i** (0.23 mmol, 23%). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 125.8, 125.9, 128.4, 129.1, 134.9, 153.9. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –179.6 (dd, J_{FF} = 32.8, 110.3 Hz, 1F, F^1), –116.4 (dd, J_{FF} = 70.8, 110.3 Hz, 1F, F^3), –101.6 (dd, J_{FF} = 32.8, 70.8 Hz, 1F, F^2).



2-(1,2,2-Trifluorovinyl)benzofuran (2j): Following the general procedure, the reaction with 5,5-dimethyl-2-benzofuryl-1,3,2-dioxaborinane (**1j**) was conducted for 0.5 h to give **2j** (0.56 mmol, 56%). ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 6.9 (s, 1H), 7.3 (m, 1H), 7.4 (m, 1H), 7.5 (d, J = 8.2 Hz, 1H), 7.6 (d, J = 7.5 Hz, 1H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 155.3, 153.5, 143.3, 127.7, 125.6, 123.7, 123.5, 121.5, 111.6, 105.9. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –186.9 (dd, J_{FF} = 29.8, 110.3 Hz, 1F, F^1), –113.9 (dd, J_{FF} = 60.6, 110.3 Hz, 1F, F^3), –100.4 (dd, J_{FF} = 29.8, 60.6 Hz, 1F, F^2). HRMS Calcd for $C_{10}H_5F_3O$ 198.0292, Found *m/z* 198.0286.



2-(1,2,2-Trifluorovinyl)benzothiophene (2k): Following the general procedure, the reaction with 5,5-dimethyl-2-benzothienyl-1,3,2-dioxaborinane (**1k**) was conducted for 0.5 h to give **2k** (0.58 mmol, 58%). ^{19}F NMR (376 MHz, THF/THF-d_8, rt, δ/ppm): –173.7 (dd, J_{FF} = 31.6, 109.4 Hz, 1F, F^1), –114.5 (dd, J_{FF} = 64.1, 109.4 Hz, 1F, F^3), –102.2 (dd, J_{FF} = 31.6, 64.1 Hz, 1F, F^2).



(*E*)-1,1,2-trifluorodeca-1,3-diene (2l): Following the general procedure, the reaction with (*E*)-5,5-dimethyl2-(oct-1-en-1-yl)-1,3,2-dioxaborinane (**1l**) was conducted for 0.5 h. The crude yield determined by ^{19}F NMR was 73%. Attempt to isolation of the product was hampered by its extremely higher vapor pressure. ^{19}F NMR (376 MHz, THF/THF-d_8, rt, δ/ppm): –183.8 (dddm, J_{HF} = 26.7 Hz, J_{FF} = 28.0, 106.2 Hz, 1F, F^1), –124.4 (dd, $_{FF}$ = 73.2, 106.2 Hz, 1F, F^3), –105.6 (dd, J_{FF} = 28.0, 73.2 Hz, 1F, F^2).

Preparation of 3 (Scheme 2.5): $Pd(PCy_3)_2$ (930 mg, 1.39 mmol) was dissolved into 10 mL of toluene. The pale yellow solution was transferred into a reaction vial equipped with a J-Young valve. The reaction vial was degassed. TFE (1 atm) was charged into the vial, and the reaction mixture was stirred at ambient temperature for 5 h. Gradual formation of white precipitate was observed. All volatiles were removed under reduced pressure, and then white residue was washed with hexane, affording 877 mg of **3** (1.13 mmol, 81%) as white solid. Single crystals for X-ray diffraction analysis were prepared by recrystallization from toluene/hexane at –30ºC. ^{1}H NMR (400 MHz, C_6D_6, rt, δ/ppm): 1.12-1.32 (m, 9H), 1.50-1.68 (m, 9H), 1.68-1.82 (m, 6H), 2.00-2.10 (m, 9H). $^{13}C\{^1H\}$ NMR (100.6 MHz, C_6D_6, rt, δ/ppm): 26.8 (s), 28.1 (d, J_{PC} = 10.2 Hz), 30.9 (s), 36.6 (d, J_{PC} = 11.7 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, C_6D_6, rt, δ/ppm): 33.6 (m). $^{19}F\{^1H\}$ NMR (376MHz, C_6D_6, rt, δ/ppm): –128.5 (br). Anal. Calcd for $C_{38}H_{66}F_4P_2Pd$: C, 59.48; H, 8.67. Found: C, 59.61; H, 9.16. X-ray data for **1a**·2.5(C_6H_6). M = 962.52**,** colorless, Triclinic, P-1 (No. 2), a = 9.5719(10) Å, b = 11.2741(12) Å, c = 23.046(2) Å, α = 87.796(3)°, β = 88.292(4)°, γ = 89.900(4)°, V = 2484.1(5) Å^3, Z = 2, D_{calcd} = 1.287 g/cm^3, T = –150(2) °C, R_1 (wR_2) = 0.036 (0.084).

Heating of 3 (Scheme 2.6): Complex **3** (15.3 mg, 0.02 mmol) was dissolved into 0.5 mL of THF/THF-d_8 (v/v' = 4:1). The resulting solution was transferred into a pressure-tight NMR tube, and TFE (3.5 atm) was charged. After heating of the reaction mixture at 100 °C for 4 h, ^{19}F and ^{31}P NMR analysis indicated that the complete consumption of **3** and the formation of **4** and **5**. Isolation of the compounds **4** was conducted by recrystallization from THF or by following the reported method.[25] ^{1}H NMR (400 MHz, C_6D_6, rt, δ/ppm): 1.18-1.38 (m, 9H), 1.60-1.70 (m, 3H), 1.70-1.90 (m, 12H), 2.05-2.25 (m, 6H), 2.30-2.42 (m, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, C_6D_6, rt, δ/ppm): 26.7, 27.9, 30.6 (d, J_{PC} = 6.0 Hz), 34.3 (t, J_{PC} = 9.6 Hz). $^{31}P\{^1H\}$ NMR (162 MHz, C_6D_6, rt, δ/ppm): 30.0 (m). $^{19}F\{^1H\}$ NMR (376 MHz, C_6D_6, rt, δ/ppm): –99.7 (ddt, J_{FF} = 30.1, 105.4, J_{PF} = 7.3 Hz, 1F, –CF=CF*F*), –131.1 (dd, J_{FF} = 105.4, 105.4 Hz, 1F, –CF=C*F*F), –149.4 (dd, J_{FF} = 30.1, 105.4, 1F, –C*F*=CFF), –316.6 (br, 1F, Pd–*F*). Anal. Calcd for $C_{38}H_{66}F_4P_2Pd$: C, 59.48; H, 8.67. Found: C, 58.63; H, 9.26. X-ray data for **2**. M = 767.25**,** colorless, Triclinic, *Pbca* (No. 61), a = 15.6637(8) Å, b = 19.5786(9) Å, c = 24.5171(12) Å, 7518.7(6) Å^3, Z = 8, D_{calcd} = 1.356 g/cm^3, T = –150(2) °C, R_1 (wR_2) = 0.065 (0.182).

Reaction of 4 with 1a in the presence of DBA (Scheme 2.7): A mixture of **4** (15.2 mg, 0.02 mmol), **1a** (38.0 mg, 0.20 mmol), and DBA (46.2 mg, 0.20 mmol) was dissolved into 0.5 mL of THF-d_8. The reaction mixture was heated at 100 °C. ^{19}F NMR analysis revealed that the starting material **2** was completely consumed within 1 h to afford **1a** in 95% yield. Concomitant formations of **6** and (η^2-dba)Pd(PCy_3)$_2$ was observed by means of ^{11}B, ^{19}F, and ^{31}P NMR spectroscopy.

Pd(0)-catalyzed coupling reaction of 1,1-difluoroethylene with 1b (Scheme 2.11): A mixture of **1b** (240.0 mg, 1.00 mmol), $Pd_2(dba)_3(C_6H_6)$ (10.0 mg, 0.01 mmol), and P^iPr_3 (6.4 mg, 0.04 mmol) was dissolved in 10.0 mL of THF. The resulting solution was transferred into an autoclave reactor, and then 1,1-difluoroethylene (3.5 atm) was charged into the reactor. The reaction mixture was heated at 100 ºC for 6 h. After the unreacted 1,1-difluoroethylene was purged from the reactor, the reaction mixture was concentrated under reduced pressure. Pentane was added to the residue, and the resulting suspension was filtered through a short silica column. The filtrate was concentrated under reduced pressure to afford 1-(1-fluorovinyl)naphthalene (146.4 mg, 85%) as an analytically pure sample. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.93 (dd, J = 2.9, 48.4 Hz, 1H), 5.21 (dd, J = 2.9, 16.5 Hz, 1H), 7.40-7.76 (m, 4H), 7.92 (m, 2H), 8.21 (m, 1H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –90.3 (dd, J_{FH} = 16.5, 48.4 Hz). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 95.1, 125.1, 125.6, 126.3, 126.9, 127.4, 128.5, 130.4, 130.7, 130.8, 133.7, 164.1.

Pd(0)-catalyzed coupling reaction of hexafluoropropene with 1b (Scheme 2.12): A mixture of **1b** (240.0 mg, 1.00 mmol), $Pd_2(dba)_3(C_6H_6)$ (50.0 mg, 0.05 mmol), and P^nBu_3 (40.0 mg, 0.20 mmol) was dissolved in 10.0 mL of THF. The resulting solution was transferred into an autoclave reactor, and then hexafluoropropene (3.5 atm) was charged into the reactor. The reaction mixture was heated at 100 ºC for 2 h. After the unreacted hexafluoropropene was purged from the reactor, the reaction mixture was concentrated under reduced pressure. Pentane was added to the residue, and the resulting suspension was filtered through a short silica column. Further purification by column chromatography (SiO_2, hexane:EtOAc = 99:1) gave the 1-(1-naphthyl)-1,2,3,3,3-pentafluoro-1-propene in 72% yield as a stereoisomer mixture (E/Z = 16/56). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): For Z: –66.2 (dd, J_{FF} = 8.2, 13.7 Hz, 3F), –104.4 (m, 1F), –152.8 (dq, J_{FF} = 13.7, 13.7 Hz, 1F). For E: –67.1 (dd, J_{FF} = 11.2, 21.6 Hz, 3F), –126.7 (qd, J_{FF} = 21.6, 143.1 Hz, 1F), –166.4 (qd, J_{FF} = 11.2, 143.1 Hz, 1F).

Reaction of octafluorotoluene with 1c (Scheme 2.13): A mixture of octafluorotoluene (118.0 mg, 0.50 mmol), **1c** (110.0 mg, 0.50 mmol), and [Ni(^{i}Pr$_2$Im)$_2$]$_2$(cod) (20.8 mg, 0.025 mmol) was dissolved in 2.0 mL of THF. The reaction mixture was heated at 100 ºC for 10 h, and concentrated under reduced pressure. Pentane was added to the residue, and the resulting suspension was filtered through a short silica column to afford 2,3,5,6-tetrafluoro-4-trifluoromethyl-4'-methoxybiphenyl (141.0 mg, 87%) as an analytically pure white solid. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 3.98 (s, 3H), 7.02 (d, J = 8.7 Hz, 2H), 7.42 (d, J = 8.7 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –56.2 (t, J_{FF} = 21.6 Hz, 3F), –141.2 (m, 2F), –142.1 (m, 2F).

Reaction of hexafluorobenzene with 1c (Scheme 2.13): A mixture of hexafluorobenzene (93.0 mg, 0.50 mmol), **1c** (110.0 mg, 0.50 mmol), and [Ni(^{i}Pr$_2$Im)$_2$]$_2$(cod) (20.8 mg, 0.025 mmol) was dissolved in 2.0 mL of THF. The reaction mixture was heated at 100 ºC for 10 h, and concentrated under reduced pressure. Pentane was added to the residue, and the resulting suspension was filtered through a short silica column to afford 2,3,4,5,6-pentafluoro-4'-methoxybiphenyl (47.4 mg, 35%) as an analytically pure white solid. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 3.95 (s, 3H), 7.01 (d, J = 8.7 Hz, 2H), 7.43 (d, J = 8.7 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –143.6 (dd, J_{FF} = 8.6, 23.4 Hz, 1F), –156.5 (t, J_{FF} = 21.0 Hz, 1F), –162.6 (m, 2F).

Reaction of fluorobenzene with 1c (Scheme 2.13): A mixture of **1c** (110.0 mg, 0.50 mmol) and [Ni(^{i}Pr$_2$Im)$_2$]$_2$(cod) (20.8 mg, 0.025 mmol) was dissolved in 1.0 mL of fluorobenzene. The reaction mixture was heated at 100 ºC for 10 h, and concentrated under reduced pressure. The formation of 4-methoxybiphenyl (35%) was confirmed by GC analysis. Further purification by column chromatography (SiO_2, hexane:EtOAc = 99:1) gave the pure product (18.6 mg, 20%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 3.93 (s, 3H), 7.02 (m, 2H), 7.41 (m, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 55.5, 114.4, 126.8, 126.9, 128.3, 128.9.

2.7 References and notes

19. a) N. Miyaura, A. Suzuki, *J. C. S. Chem. Commun.* **1979**, 866. For reviews of the coupling reaction with organoboron compounds, see: b) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457; c) N. Miyaura, *J. Organomet. Chem.* **2002**, *653*, 54; d) A. Suzuki, *Angew. Chem. Int. Ed.* **2011**, *50*, 6722.

20. Some C–C bond formation reactions with organoboron compounds are known to proceed under neutral conditions, in which such an active species as a palladium alkoxy or acyl complex would be in situ generated by oxidative addition of a C–O bond, see a) L. J. Gooßen, K. Ghosh, *Angew. Chem. Int. Ed.* **2001**, *40*, 3458; b) H. Tsukamoto, M. Sato, Y. Kondo, *Chem. Commun.* **2004**, 1200.
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22. a) B. P. Carrow, J. F. Hartwig, *J. Am. Chem. Soc.* **2011**, *133*, 2116; b) C. Amatore, A. Jutand, G. Le Duc, *Chem. Eur. J.* **2012**, *18*, 6616; c) C. Amatore, A. Jutand, G. Le Duc, *Angew. Chem. Int. Ed.* **2012**, *51*, 1379.
23. Until this study, several group had reported Pd(0)- or Ni(0)-catalyzed Suzuki-Miyaura coupling of fluoroarenes via C–F bond activation, but no base-free reaction had been achieved, see: a) D. A. Widdowson, R. Wilhelm, *Chem. Commun.* **1999**, 2211; b) D. A. Widdowson, R. Wilhelm, *Chem. Commun.* **2003**, 578; c) Y. M. Kim, S. Yu, *J. Am. Chem. Soc.* **2003**, *125*, 1696; d) K. Mikami, T. Miyamoto, M. Hatano, *Chem. Commun*. **2004**, 2082; e) A. Steffen, M. Sladek, T. Braun, B. Neumann, H.-G. Stammler, *Organometallics* **2005**, *24*, 4057; f) S. Bahmanyar, B. C. Borer, Y. M. Kim, D. M. Kurtz, S. Yu, *Org. Lett*. **2005**, *7*, 1011; g) J. Liu, M. Robins, *Org. Lett*. **2005**, *7*, 1149; h) T. Schaub, M. Backes, U. Radius, *J. Am. Chem. Soc.* **2006**, *128*, 15964; i) M. R. Cargill, G. Sandford, A. J. Tadeusiak, D. S. Yufit, J. A. K. Howard, P. Kilickiran, G. Nelles, *J. Org. Chem.* **2010**, *75*, 5860; j) A. D. Sun, J. A. Love, *Org. Lett.* **2011**, *13*, 2750; k) D. Yu, Q. Shen, L. Lu, *J. Org. Chem.* **2012**, *77*, 1798; l) D. Breyer, T. Braun, P. Klaring, *Organometallics* **2012**, *31*, 1417.
24. a) T. Schaub, U. Radius, *Chem. Eur. J.* **2005**, *11*, 5024; b) T. Schaub, M. Backes, U. Radius, *J. Am. Chem. Soc.* **2006**, *128*, 15964; c) T. Schaub, P. Fischer, A. Steffen, T. Braun, U. Radius, A. Mix, *J. Am. Chem. Soc.* **2008**, *130*, 9304; d) T. Schaub, P. Fischer, T. Meins, U. Radius, *Eur. J. Inorg. Chem.* **2011**, 3122; e) P. Fischer, K. Gotz, A. Eichhorn, U. Radius, *Organometallics* **2012**, *31*, 1374.
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Chapter 3

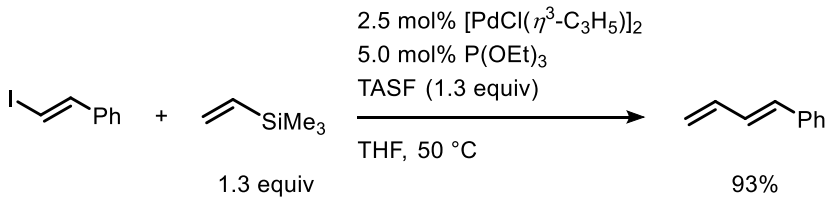
Pd(0)-Catalyzed Base-Free Hiyama Coupling of TFE

Abstract

In the presence of catalytic amount of Pd(0) and $PCyp_3$, the coupling reaction of TFE with $ArSi(OMe)_3$ took place without the addition of base to afford the TFS derivatives in good yields. This is the first base-free Hiyama coupling reaction. A fluoropalladium(II) complex generated by the oxidative addition of a C-F bond of TFE is reactive enough toward non-activated $ArSi(OMe)_3$, which enables the catalytic reaction to proceed without base. The base-free system is applicable to the coupling reaction using fluoroarenes.

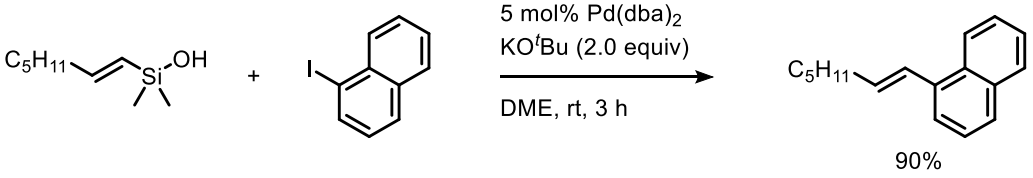
3.1 Introduction

Among the transition-metal catalyzed C–C bond formation reactions, the Hiyama coupling reaction of organic halides with organosilicon reagents has garnered a great deal of interest in recent years, due to the ease of preparation, stability, and environmentally benign nature of organosilicon reagents. Since the pioneering works accomplished by Hiyama, several groups have reported various modifications with functionalized organosilicon reagents.[26] These reactions generally require an activator to enhance the reactivity of an organosilicon reagent, which is achieved by the addition of a fluoride anion source such as TASF and TBAF.

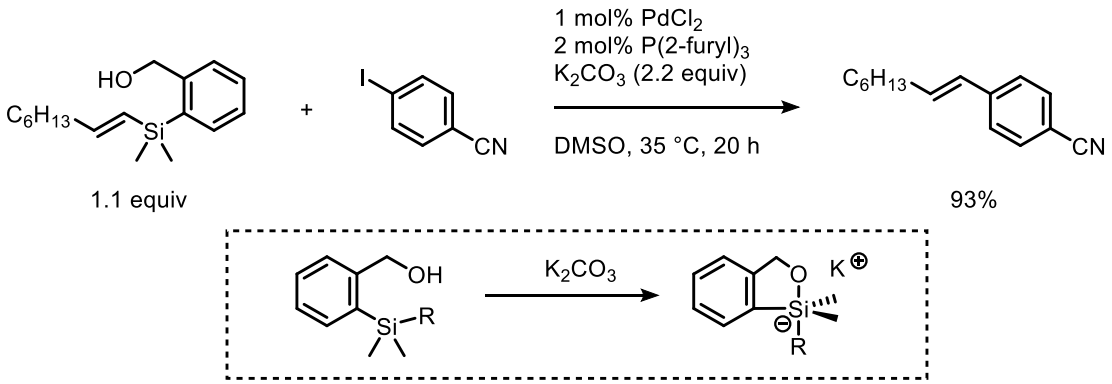


Scheme 3.1. Seminal work for Pd(0)-catalyzed Hiyama coupling reaction.[26a]

Recent developments have made this reaction possible with the aid of a Brønsted base instead of the fluoride anion. For example, Dennmark developed the coupling reaction using alkenylsilanols with KO^{t}Bu as an activator (Scheme 3.2).[26e] Nakao and Hiyama reported the coupling reaction using [2-(hydroxymethyl)phenyl]dimethylsilanes, which are possible to be activated by K_2CO_3 (Scheme 3.3).[26g] These methods are called "fluoride-free" Hiyama coupling reactions and have attracted much attention for decades.[27]

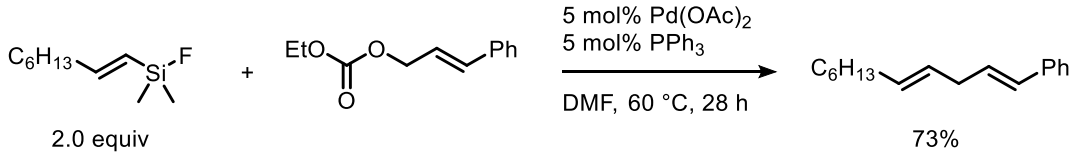


Scheme 3.2. Hiyama coupling with alkenylsilanol.[26e]



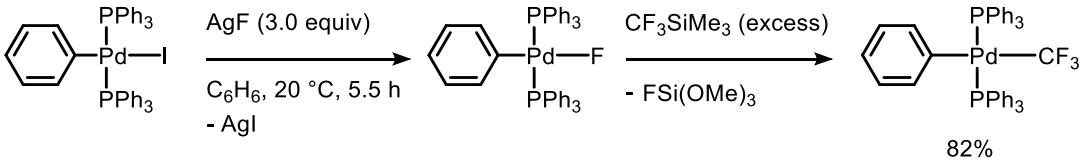
Scheme 3.3. Hiyama coupling with [2-(hydroxymethyl)phenyl]dimethylsilanes.[26g]

On the other hand, little is known about "base-free" Hiyama coupling reaction. To the best of our knowledge, base-free C–C bond formation reactions of organosilicon reagents have been achieved only while using allylic carbonate or vinyl oxirane as a substrate (Scheme 3.4).[28] These reactions would proceed via η^3-allylpalladium alkoxide intermediates, which are considered to be an activator for neutral organosilicon reagents. However, base-free reactions using alkenyl or aryl halides as substrates have not been reported, except for those using preliminarily activated organosilicon reagent.[29]

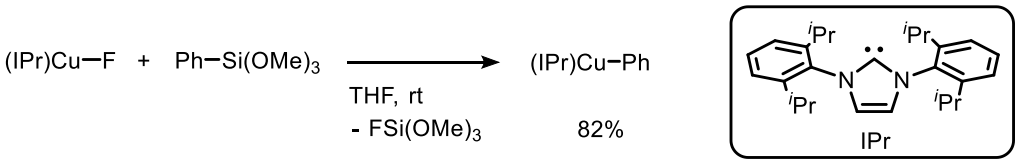


Scheme 3.4. Reaction of allylic carbonate with alkenylfluorosilane.[28a]

In general, neutral organosilicon reagents are less reactive than activated silicate species, however, transition metal fluoride complexes are considered to have high reactivity toward neutral organosilicon reagents. In fact, the transmetalation of a transition metal fluoride complex with an organosilicon reagent [$XSiR_3$] (X = H, Cl, OTf, CF_3, etc.) is a well-established method for the synthesis of various kinds of transition metal complexes [$L_nTm–X$].[30] For example, for the synthesis of $(PPh_3)_2Pd(CF_3)Ph$, Grushin conducted the reaction of $(PPh_3)_2Pd(F)Ph$ with $PhSi(OMe)_3$ (Scheme 3.5).[30a] Although aryl group transfer (X = Ar) has remained less-developed due to a relatively inert Si–C bond, in 2008, Ball demonstrated the reaction of (IPr)CuF with $ArSi(OMe)_3$ for the synthesis of the corresponding organocopper reagents.[30d]

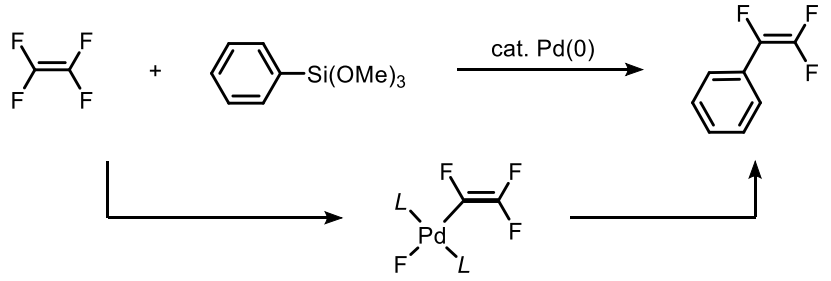


Scheme 3.5. Synthesis of $(PPh_3)_2Pd(CF_3)Ph$ through $(PPh_3)_2Pd(F)Ph$.[30a]



Scheme 3.6. Reaction of (IPr)CuF with $PhSi(OMe)_3$.[30d]

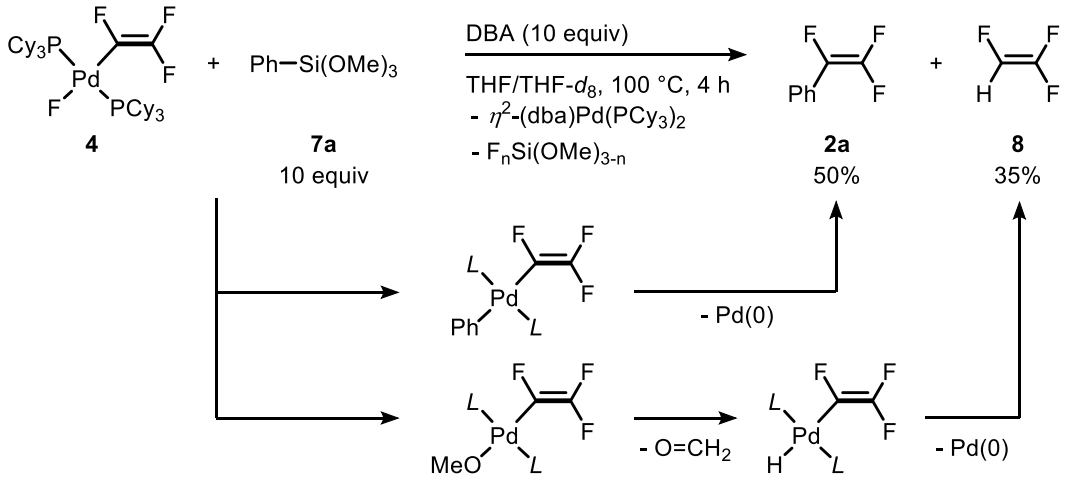
Against the aforementioned research backgrounds, developed in this study was a base-free Hiyama coupling reaction of TFE via an fluoropalladium(II) intermediate generate by the oxidative addition of C–F bond. The coupling reaction proceeded without base due to high reactivity of fluoropalldium(II) intermediate toward neutral organosilicon reagents (Scheme 3.7).



Scheme 3.7. Pd(0)-catalyzed base-free Hiyama coupling of TFE with $PhSi(OMe)_3$.

3.2 Stoichiometric reactions

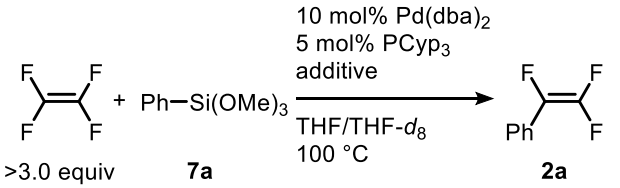
First, the reactivity of *trans*-$(PCy_3)_2Pd(F)(CF{=}CF_2)$ (**4**) toward organosilicon compounds was investigated. In the presence of DBA, the reaction of **4** with 10 equiv of $PhSi(OMe)_3$ **7a** in THF at 100 °C proceeded to afford trifluorostyrene (**2a**) and trifluoroethylene (**8**) in 50% and 35%, respectively, with the concomitant formations of fluorosilanes $F_nSi(OMe)_{3-n}$ (Scheme 3.8). In this reaction, **2a** was generated via transmetalation and following reductive elimination. On the other hand, **8** would be generated as a result of a methoxy group transfer, following *β*-hydrogen elimination and reductive elimination.



Scheme 3.8. Reaction of **4** with **7a** in the absence of base.

3.3 Development of the catalytic reaction

After a series of survey on the reaction conditions, it was found that the base-free Hiyama coupling reaction of TFE with $PhSi(OMe)_3$ (**7a**) proceeded smoothly in the presence of 2.5 mol% of $Pd_2(dba)_3(C_6H_6)$ and 5 mol% of $PCyp_3$ (Table 3.1, entry 1). In the catalytic reactions, only a small amount of **8** was observed unlike the stoichiometric reaction shown in Scheme 3.8. Interestingly, the time-product yield curve of this catalytic reaction resembled that observed in an auto-catalytic reaction (Figure 3.1, A). The generation rate of **2a** was slow at the early stage of the reaction, and then increased sharply at some point. It is assumed that the increase was caused by the fluorosilanes that were generated in situ as the coupling reaction proceeded. In fact, by using 10 mol% of $FSi(OEt)_3$ as an additive, the reaction was obviously accelerated (Figure 3.1, B), and the yield of **2a** was increased to 91% (Table 3.1, entry 2). On the other hand, when the reactions was conducted with other additives, the yield decreased (entries 3-6).



entry	additive	time	yield
1	none	4 h	76%
2	10 mol% $FSi(OEt)_3$	6 h	91%
3	10 mol% TBAF	6 h	0%
4	1.0 equiv TBAF	6 h	0%
5	1.0 equiv Cs_2CO_3	5 h	49%
6	1.0 equiv LiI	6 h	0%

Yields were determined by ^{19}F NMR.

Table 3.1. Optimization of the reaction conditions.

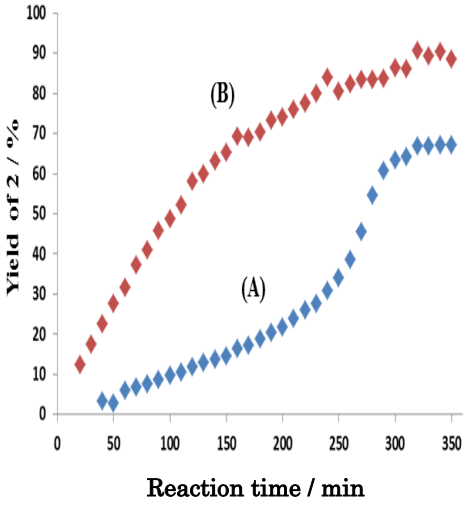
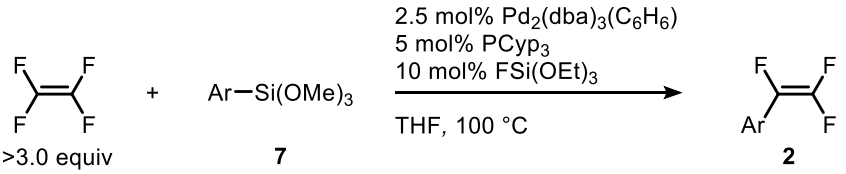
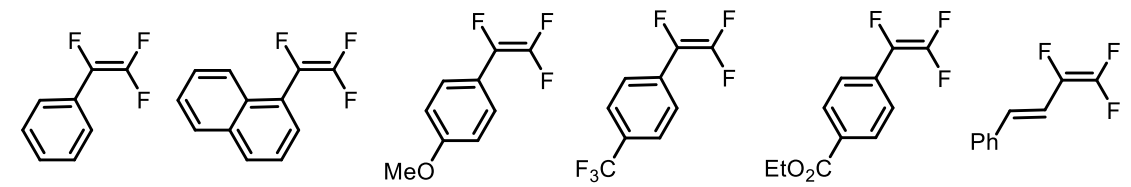


Figure 3.1. Time-yield profile of the catalytic reaction. (A) entry 1. (B) entry 2.

With the optimized reaction conditions, the scope of the reaction was investigated (Table 3.2). In the presence of 2.5 mol% $Pd_2(dba)_3(C_6H_6)$, 5 mol% $PCyp_3$, and 10 mol% of $FSi(OEt)_3$, the coupling reaction of TFE with $PhSi(OMe)_3$ occurred at 80 °C to give **2a** in 94% yield. Sterically-hindered trimethoxy(naphthalene-1-yl)silane was converted into **2b** in high yield. The reaction with electron-rich arylsiloxane required high catalyst loading to furnish **2c** in 57% yield. On the other hand, electron-deficient arylsiloxanes were smoothly converted into the corresponding products (**2d** and **2m**). An alkenylsiloxane was also applicable to this coupling reaction (**2n**).

Table 3.2. Substrate scope of Pd(0)-catalyzed base-free Hiyama coupling of TFE.



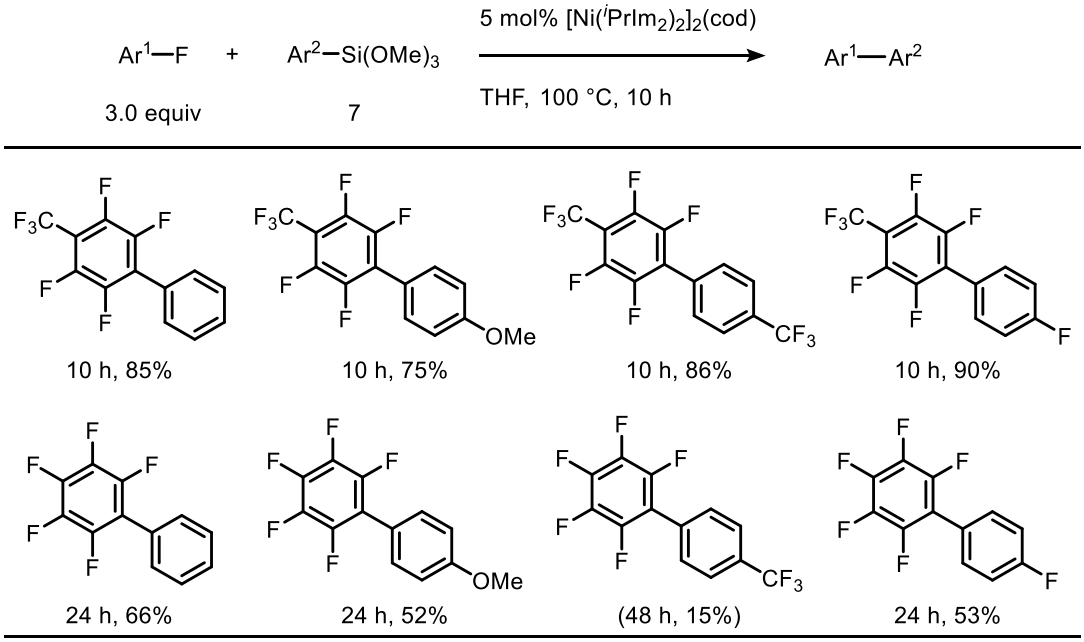


2a	**2b**	**2c**	**2d**	**2m**	**2n**
(23 h, 94%)[a]	20 h, 72%	24 h, 57%[b]	(8 h, 75%)[a]	24 h, 72%	24 h, 40%[a]

Isolated yields. Values in parentheses are NMR yields determined by ^{19}F NMR. (a) Heated at 80 °C. (b) Conducted with 5 mol% of $Pd_2(dba)_3(C_6H_6)$, 10 mol% of $PCyp_3$, and 20 mol% of $FSi(OEt)_3$.

Furthermore, the base-free Hiyama coupling was found to be applicable to fluoroarenes, by using $[Ni(^{i}PrIm_2)_2]_2(cod)$ as the catalyst (Tale 3.3). The results of Ni(0)-catalyzed base-free Hiyama coupling of octafluorotoluene or hexafluorobenzene were summarized in Table 3.3. The reactions using octafluorotoluene proceeded smoothly to afford the corresponding biaryls in high yields. The reaction using hexafluorobenzene gave the coupling products in moderate yields. Unlike the case of the reaction with TFE as a substrate, neither the reaction rate nor the yield was improved by the addition of $FSi(OEt)_3$.

Table 3.3. Ni(0)-catalyzed base-free Hiyama coupling of octafluorotoluene or hexafluorobenzene.



Isolated yields. Value in parenthesis is NMR yield determined by ^{19}F NMR.

3.4 Conclusion

In chapter 3, a Pd(0)-catalyzed base-free Hiyama coupling reaction of TFE was described. This is the first example of the Hiyama coupling reaction without base. It was also found that fluorosilanes accelerated the catalytic reaction. A fluoropalladium(II) complex generated by the oxidative addition of C–F bond would play an essential role in the base-free reaction. Furthermore, the base-free system was found to be applicable to fluoroarenes by using Ni(0)/NHC catalyst.

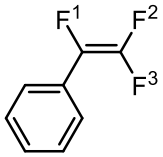
3.5 Experimental section

Reaction of 4 with 7a in the presence of DBA (Scheme 3.7): A mixture of **4** (15.2 mg, 0.02 mmol), $PhSi(OMe)_3$ (**7a**: 39.6 mg, 0.20 mmol), and DBA (46.2 mg, 0.20 mmol) was dissolved into 0.5 mL of THF-d_8. The reaction mixture was heated at 100 °C for 4 h. ^{19}F NMR analysis revealed that the starting material **2** was completely consumed within 1 h to afford **1a** in 95% yield. Concomitant formations of **6** and (η^2-dba)$Pd(PCy_3)_2$ was observed by means of ^{11}B, ^{19}F, and ^{31}P NMR spectroscopy.

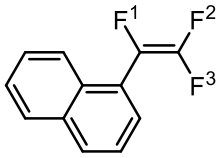
General procedure for the optimization of the reaction conditions (Table 3.1): The reaction was conducted with a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7). A mixture of **7a** (19.8 mg, 0.10 mmol), $Pd_2(dba)_3(C_6H_6)$ (2.50 mg, 0.0025 mmol), $PCyp_3$ (1.19 mg, 0.0050 mmol), and additive was dissolved in 0.50 mL of THF/THF-d_8 (v/v' = 4/1). The resulting solution was transferred into the tube, and then TFE (3.5 atm, >0.30 mmol) was charged. The reaction mixture was heated at 100 ºC until the reaction was terminated. Monitoring the reaction was performed by means of ^{19}F NMR spectroscopy. Yield was determined by ^{19}F NMR with $PhCF_3$ as an internal standard.

Plotting the yield of 2a against reaction time (Figure 3.1): The reactions were conducted with a pressure-tight NMR tube. A mixture of $PhSi(OMe)_3$ (19.8 mg, 0.10 mmol), $Pd_2(dba)_3(C_6H_6)$ (2.50 mg, 0.0025 mmol), and $PCyp_3$ (1.19 mg, 0.0050 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. Then, the tube was introduced into a thermostated NMR probe at 100 ºC. Monitoring the reaction and estimating the yield were performed within 10 minutes of each other by means of ^{19}F NMR spectroscopy.

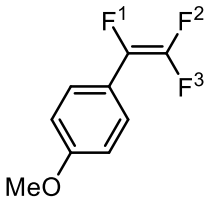
General procedure for the isolation of trifluorostyrenes (2): The reactions were conducted with an autoclave reactor. A mixture of $ArSi(OMe)_3$ (1.0 mmol), $Pd_2(dba)_3(C_6H_6)$ (25.0 mg, 0.025 mmol), $PCyp_3$ (11.9 mg, 0.050 mmol), and $FSi(OEt)_3$ (18.3 mg, 0.10 mmol) was dissolved in 5.0 mL of THF. The resulting solution was transferred into the autoclave reactor, and then TFE (3.5 atm) was charged. The reaction mixture was heated at 100 ºC for the given time. After the unreacted TFE was purged from the reactor, the reaction mixture was concentrated under reduced poressure. Then, 10.0 mL of pentane was added to the residue, and the resulting suspension was filtered through a short silica column. Further purification was conducted by HPLC ($CHCl_3$).



***α,β,β*-Trifluorostyrene (2a)**: Following the general procedure, the reaction with trimethoxy(phen)silane (19.8 mg, 0.10 mmol) was conducted at 80 °C. The formation of **2a** (0.094 mmol, 94%) was confirmed by ^{19}F NMR and GCMS analysis. ^{19}F NMR (376 MHz, THF/THF-d_8, rt, δ/ppm): –179.0 (dd, J_{FF} = 32.7, 110.3 Hz, 1F, F^1), –118.5 (dd, J_{FF} = 73.5, 110.3 Hz, 1F, F^3), –104.2 (dd, J_{FF} = 32.7, 73.5 Hz, 1F, F^2).



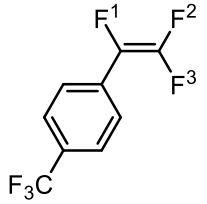
1-(1,2,2-Trifluorovinyl)naphthalene (2b): Following the general procedure, trimethoxy(naphthalen-1-yl)silane (248 mg, 1.0 mmol) was converted into the title compound (150 mg, 72%) as a white solid. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.50-8.05 (m, 7H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 123.8 (dd, J_{CF} = 20.0, 4.0 Hz), 124.9 (d, J_{CF} = 2.8 Hz), 125.1 (d, J_{CF} = 1.2 Hz), 126.7, 127.4, 127.9 (ddd, J_{FF} = 232.4, 50.8, 19.8 Hz), 128.7, 128.9 (m), 131.4, 131.4, 133.7 (d, J_{CF} = 1.6 Hz), 154.0 (ddd, J_{FF} = 290.2, 282.5, 49.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –159.8 (dd, J_{FF} = 117.7, 29.8 Hz, 1F, F^1), –117.0 (dd, J_{FF} = 117.7, 75.2 Hz, 1F, F^3), –101.4 (dd, J_{FF} = 75.2, 29.8 Hz, 1F, F^2).



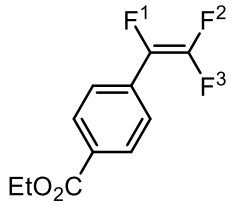
1-Methoxy-4-(1,2,2-trifluorovinyl)benzene (2c):

Following a modification of the general procedure (using 5 mol% of $Pd_2(dba)_3(C_6H_6)$, 10 mol% of $PCyp_3$ and 20 mol% of $FSi(OEt)_3$), trimethoxy(4-methoxyphenyl)silane (228 mg, 1.0 mmol) was converted into the title compound (107 mg, 57%) as a colorless oil. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 3.84 (s, 3H), 6.95 (d, J_{HH} = 8.6 Hz, 2H), 7.41 (d, J_{HH} = 8.6 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 55.2, 114.1, 119.6 (dd, J_{CF} = 22.7, 6.6 Hz), 126.1(m), 128.7 (ddd, J_{FF} = 225.9, 46.0, 19.8

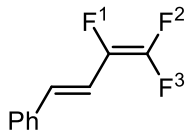
Hz), 153.4 (ddd, J_{FF} = 288.0, 282.8, 51.1 Hz), 159.9. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –175.4 (dd, J_{FF} = 110.0, 31.7 Hz, 1F, F^1), –114.3 (dd, J_{FF} = 110.0, 77.7 Hz, 1F, F^3), –99.1 (dd, J_{FF} = 77.7, 31.7 Hz, 1F, F^2).



1-Trifluoromethyl-4-(1,2,2-trifluorovinyl)benzene (2d): Following the general procedure, the reaction with trimethoxy(4-(trifluoromethyl)phenyl)silane (26.6 mg, 0.10 mmol) was conducted at 80 °C. The formation of **2d** (0.075 mmol, 75%) was confirmed by ^{19}F NMR and GCMS analysis. ^{19}F NMR (376 MHz, THF/THF-d_8, rt, δ/ppm): –179.8 (dd, J_{FF} = 32.7, 109.2 Hz, 1F, F^1), –115.0 (dd, J_{FF} = 65.3, 109.2 Hz, 1F, F^3), –100.8 (dd, J_{FF} = 32.7, 65.3 Hz, 1F, F^2).



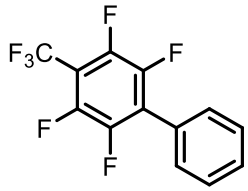
Ethyl 4-(1,2,2-trifluorovinyl)benzoate (2m): Following the general procedure, ethyl 4-(trimethoxysilyl)benzoate (270 mg, 1.00 mmol) was converted the title compound (166 mg, 72%) as a colorless oil. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 1.39 (t, J = 7.2 Hz), 4.38 (q, J = 7.2 Hz), 7.51 (d, J = 8.5 Hz, 2H), 8.07 (d, J_{HH} = 8.5 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 14.1, 61.1, 123.9 (m), 128.1 (ddd, J_{CF} = 227.1, 44.6, 19.9 Hz), 129.8, 130.5 (t, J_{CF} = 2.3 Hz), 131.3 (dd, J_{CF} = 21.9, 7.1 Hz), 154.1 (ddd, J_{CF} = 293.2, 285.2, 48.4 Hz), 165.7. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –177.5 (dd, J_{FF} = 108.5, 32.9 Hz, 1F, F^1), –111.5 (dd, J_{FF} = 108.5, 63.7 Hz, 1F, F^3), –96.9 (dd, J_{FF} = 108.5, 32.9 Hz, 1F, F^2).



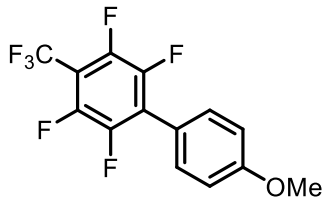
(*E*)-(4,5,5-trifluoropenta-2,4-dien-1-yl)benzene (2n): Following the general procedure,

(*E*)-trimethoxy(3-phenylprop-1-en-1-yl)silane (238 mg, 1.00 mmol) was converted into the title compound (80.0 mg, 40%) as an yellowish oil. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 3.41 (d, J_{HH} = 6.6 Hz, 2H, PhC*H*$_2$CH=CH–), 5.83 (ddm, J_{HF} = 24.9 Hz, J_{HH} = 14.9 Hz, 1H, PhCH$_2$CH=C*H*–), 6.05 (dt, J_{HH} = 14.9, 6.6 Hz, 1H, PhCH$_2$C*H*=CH–), 7.10-7.26 (m, 5H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 39.0, 115.3 (ddd, J_{CF} = 17.8, 5.3, 1.5 Hz), 126.6, 128.1 (ddd, J_{CF} = 230.3, 48.8, 19.1 Hz), 128.8, 128.8, 130.2 (ddd, J_{CF} = 12.4, 4.5, 2.1 Hz), 139.1, 152.5 (ddd, J_{CF} = 292.7, 283.2, 46.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –180.9 (ddd, J_{FF} = 107.6, 27.4 Hz, J_{HF} = 24.9 Hz, 1F, F^1), –119.9 (ddd, J_{FF} = 107.6, 69.3 Hz, J_{HF} = 2.9 Hz, 1F, F^3), –103.6 (dd, J_{FF} = 69.3, 24.9 Hz, 1F, F^2). HRMS Calcd for $C_{11}H_9F_3$ 198.0656, found *m/z* 198.0651.

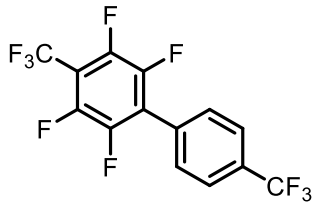
General procedure for Ni(0)-catalyzed coupling reaction of octafluorotoluene with ArSi(OMe)$_3$ (Table 3.3): A mixture of ArSi(OMe)$_3$ (0.50 mmol), octafluorotoluene (354 mg, 1.50 mmol), and [Ni$_2$(^{i}Pr$_2$Im)$_4$(ccd)] (20.8 mg, 0.025 mmol) was dissolved in 10.0 mL of THF. The reaction mixture was heated at 100 ºC for 10 h. All volatiles were removed under the reduced pressure, and then insoluble solids were filtered off with pentane to afford the coupling product. Further purification was conducted by means of flash column chromatography.



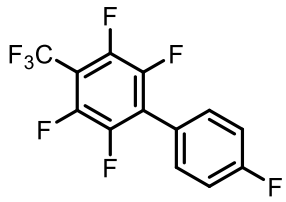
2,3,5,6-Tetrafluoro-4-trifluoromethylbiphenyl: Following the general procedure, the reaction using trimethoxy(phenyl)silane (99.1 mg, 0.50 mmol) was conducted. Further purification by means of flash column chromatography with pentane as the eluent afforded the title compound in 85% yield (125 mg). ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.45-7.53 (m, 5H). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 108.7 (m), 118.3 (q, J_{CF} = 272.8 Hz, –CF_3), 125.1 (t, J_{CF} = 16.5 Hz), 126.2, 129.0, 130.1 (t, J_{CF} = 2.0 Hz), 130.1, 144.2 (ddt, J_{CF} = 250.4 Hz, 13.2 Hz, 4.6 Hz), 144.7 (dm, J_{CF} = 259.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –144.7 (m, 2F), –143.9 (m, 2F), –59.4 (t, J_{FF} = 21.8 Hz, 3F).



2,3,5,6-Tetrafluoro-4'-methoxy-4-(trifluoromethyl)biphenyl: Following the general procedure, the reaction using trimethoxy(4-methoxyphenyl)silane (114 mg, 0.50 mmol) was conducted. Further purification by means of flash column chromatography with pentane as the eluent afforded the title compound in 75% yield (103 mg). ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 3.88 (s, 3H), 7.04 (m, 2H), 7.41 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 55.5, 114.5, 118.2, 131.6, 161.0. Signals assigned to the $C_6F_4CF_3$ group could not be clearly detected due to multiple ^{13}C-^{19}F couplings. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –142.1 (m, 2F), –141.1 (m, 2F), –56.2 (t, J_{FF} = 21.9 Hz, 3F).

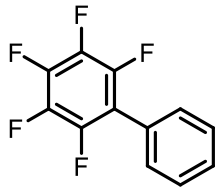


2,3,5,6-Tetrafluoro-4,4'-bis(trifluoromethyl)biphenyl: Following the general procedure, the reaction of trimethoxy(4-(trifluoromethyl)phenyl)silane (133 mg, 0.50 mmol) was conducted. Further purification by means of flash column chromatography with pentane as the eluent afforded the title compound in 86% yield (156 mg). ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.61 (d, J = 8.1 Hz, 2H), 7.80 (d, J = 8.1 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 109.6 (m), 120.9 (q, J_{CF} = 275.6 Hz, –CF_3), 123.6 (t, J_{CF} = 16.2 Hz), 123.8 (q, J_{CF} = 273.4 Hz, –CF_3), 126.1 (q, J_{CF} = 3.9 Hz), 129.9 (m), 130.7 (t, J_{CF} = 1.9 Hz), 132.2 (q, J_{CF} = 31.9 Hz), 144.4 (ddt, J_{CF} = 250.8 Hz, 13.0 Hz, 4.9 Hz), 144.8 (dm, J_{CF} = 259.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –144.3 (m, 2F), –143.0 (m, 2F), –66.2 (s, 3F), –59.5 (t, J_{FF} = 21.7 Hz, 3F). HRMS Calcd for $C_{14}H_4F_{10}$ 362.0153 found *m/z* 362.0157.



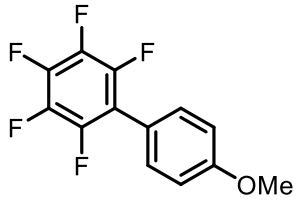
2,3,4',5,6-Pentafluoro-4-(trifluoromethyl)biphenyl: Following the general procedure, the reaction of trimethoxy(4-fluorophenyl)silane (108 mg, 0.50 mmol) was conducted. Further purification by means of flash column chromatography with pentane as the eluent afforded the title compound in 90% yield (140 mg). ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.23 (m, 2H), 7.47 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 108.9 (m), 116.4 (d, J_{CF} = 22.3 Hz), 121.0 (qt, J_{CF} = 276.1 Hz, 1.2 Hz, –CF_3), 122,4 (m), 124.1 (t, J_{CF} = 17.8 Hz), 132.2 (dt, J_{CF} = 8.7 Hz, 2.0 Hz), 144.4 (ddt, J_{CF} = 249.5 Hz, 13.8 Hz, 4.6 Hz), 144.8 (dm, J_{CF} = 260.0 Hz), 164.2 (d, J_{CF} = 254.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –144.7 (m, 2F), –143.7 (m, 2F), –113.0 (m, 1F), –59.4 (t, J_{FF} = 21.8 Hz, 3F). HRMS Calcd for $C_{13}H_4F_8$ 312.0185, found *m/z* 312.0183.

General procedure for Ni(0)-catalyzed coupling reaction of hexafluorobenzene with ArSi(OMe)$_3$ (Table 3.3): A mixture of $ArSi(OMe)_3$ (0.20 mmol), hexafluorobenzene (112 mg, 0.60 mmol), and $[Ni_2(^{i}Pr_2Im)_4(ccd)]$ (8.3 mg, 0.010 mmol) was dissolved in 2.0 mL of THF. The reaction mixture was heated at 100 ºC for 24 h. All volatiles were removed under the reduced pressure, and then insoluble solids were filtered off with pentane to afford the coupling product. Further purification was conducted by means of flash column chromatography.

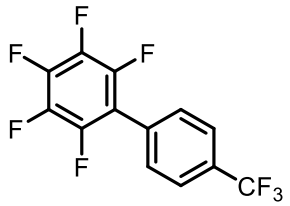


2,3,4,5,6-Pentafluorobiphenyl: Following the general procedure, the reaction using trimethoxy(phenyl)silane (39.7 mg, 0.20 mmol) was conducted. Further purification by means of flash column chromatography with hexane as the eluent afforded the title compound in 66% yield (32.3 mg). ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.39-7.53 (m, 4H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 126.4, 128.7, 129.3, 130.1. Signals assigned to the C_6F_5 group could not be clearly detected due to multiple ^{13}C-^{19}F

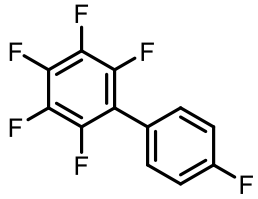
couplings. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –162.2 (m, 2F), –155.6 (t, J_{FF} = 21.0 Hz, 1F), –143.2 (dd, J_{FF} = 22.9, 8.2 Hz, 2F).



2,3,4,5,6-Pentafluoro-4'-methoxybiphenyl: Following the general procedure, the reaction using trimethoxy(4-methoxyphenyl)silane (45.7 mg, 0.20 mmol) was conducted. Further purification by means of flash column chromatography with hexane/EtOAc (99/1) as the eluent afforded the title compound in 52% yield (28.3 mg). ^1H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 3.86 (s, 3H, –OC*H*$_3$), 7.00-7.05 (m, 2H), 7.33-7.39 (m, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 55.3, 114.2, 118.3, 131.4, 160.2. Signals assigned to the C_6F_5 group could not be clearly detected due to multiple ^{13}C-^{19}F couplings. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –162.5 (m, 2F), –156.5 (t, J_{FF} = 21.1 Hz, 1F), –143.6 (dd, J_{FF} = 23.2, 7.9 Hz, 2F).



2,3,4,5,6-Pentafluoro-4'-trifluoromethylbiphenyl: Following the general procedure, the reaction of trimethoxy(4-(trifluoromethyl)phenyl)silane (53.3 mg, 0.20 mmol) was conducted. The formation of the title compound (0.030 mmol, 15%) was confirmed by ^{19}F NMR and GCMS. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –161.3 (m, 2F), –153.7 (t, J_{FF} = 20.9 Hz, 1F), –142.9 (dd, J_{FF} = 22.5, 9.1 Hz, 2F), –62.9 (s, 3F). MS (EI): *m/z* (%): 312 (100) [M]+, 262 (22), 242 (13).



2,3,4,4',5,6-Hexafluoro-1,1'-biphenyl: Following the general procedure, the reaction

of trimethoxy(4-fluorophenyl)silane (43.2 mg, 0.20 mmol) was conducted. Further purification by means of flash column chromatography with hexane as the eluent afforded the title compound in 53% yield (27.6 mg). ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.16-7.23 (m, 2H), 7.37-7.45 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$, rt, δ/ppm): 116.0 (d, J_{CF} = 21.9 Hz), 122.2, 132.0 (d, J_{CF} = 8.4 Hz), 163.1 (d, $^{1}J_{CF}$ = 249.7 Hz). Signals assigned to the C_6F_5 group could not be clearly detected due to multiple ^{13}C-^{19}F couplings. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –162.0 (m, 2F), –155.2 (t, J_{FF} = 21.2 Hz, 1F), –143.3 (dd, J_{FF} = 22.8, 8.2 Hz, 2F), –111.3 (tt, J_{HF} = 5.5, 8.3 Hz, 1F, C_6H_4F).

3.6 References and notes

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30. For selected recent examples, see: a) V. V. Grushin, W. J. Marshall, *J. Am. Chem. Soc.* **2006**, *128*, 12644; b) T. Schaub, M. Backes, U. Radius, *Eur. J. Inorg. Chem.* **2008**, 2680; c) J. L. Klinkenberg, J. F. Hartwig, *J. Am. Chem. Soc.* **2012**, *134*, 5758; d) J. R. Herron, Z. T. Ball, *J. Am. Chem. Soc.* **2008**, *130*, 16486; e) J. R. Herron, V. Russo, E. J. Valente, Z. T. Ball, *Chem. Eur. J.* **2009**, *15*, 8713; f) W. Russo, J. R. Herron, Z. T. Ball, *Org. Lett*. **2010**, *12*, 220.

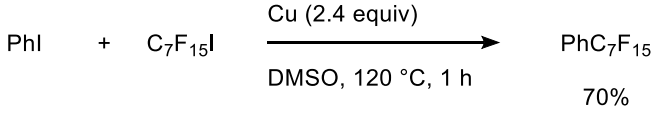
Chapter 4
Cu(I)-Mediated Construction of Tetrafluoroethylene-Bridging Structure via Carbocupration of TFE

Abstract

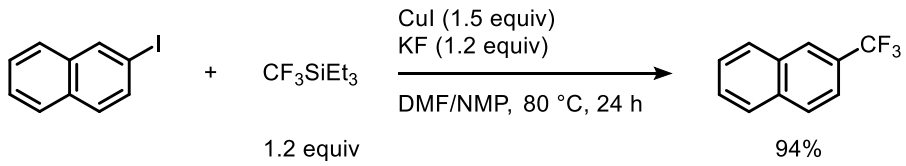
A novel synthetic method of compounds bearing tetrafluoroethylene-bridging structure via carbocupration of TFE was developed. A synthetic intermediate, 2-aryl-1,1,2,2-tetrafluoroethylcopper complexes, can be easily prepared, stored, and used as fluoroalkylation reagents. The method is applicable to the short-step synthesis of a liquid-crystalline compound bearing a tetrafluoroethylene-bridging structure.

4.1 Introduction

Since the pioneering work by McLoughlin and Thrower in 1969 (Scheme 4.1),[31] copper-mediated fluoroalkylation has been one of the most versatile methods for the introduction of fluoroalkyl groups on aromatic ring.[32] In the reaction, a fluoroalkylcopper(I) complex is considered to be a key intermediate. In 1986, Wiemers and Burton observed [CF_3Cu] species by ^{19}F NMR analysis at low temperature.[32b] Fluoroalkylcopper complexes are generally prepared via transfer of a fluoroalkyl group from a fluoroalkyl halide or fluoroalkyl silane. In particular, CF_3SiR_3, so-called Ruppert-Prakash reagent, have been widely used for the generation of [CF_3Cu] species (Scheme 4.2).[32c]

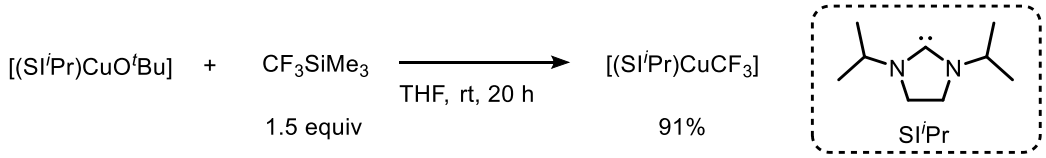


Scheme 4.1. Pioneering work for Cu(I)-mediated fluoroalkylation.[31]

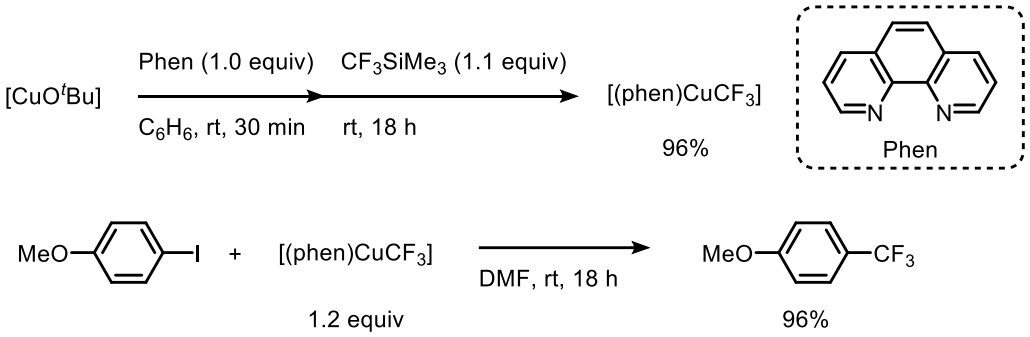


Scheme 4.2. Cu(I)-mediated trifluoromethylation with CF_3SiEt_3.[32c]

Recently, several groups reported the isolations of ligand-stabilized fluoroalkylcopper complexes. Komiya reported the synthesis of $[(PPh_3)_3CuCF_3]$ by the reaction of $[(PPh_3)_3CuOPh]$ with CF_3SiMe_3 in 2000.[33] In 2008, Vicic reported the first structually-defiend $[CuCF_3]$ complex with N-heterocyclic carbene ligand, and also disclosed the trifluoromethylation reaction with the complex (Scheme 4.3).[34] Hartwig reported the synthesis of fluoroalkylcopper complexes with 1,10-phenanthroline (phen) ligand $[(phen)CuC_nF_{2n+1}]$ (n = 1−3), along with reports of outstanding performance as fluoroalkylation reagents (Scheme 4.4).[35]

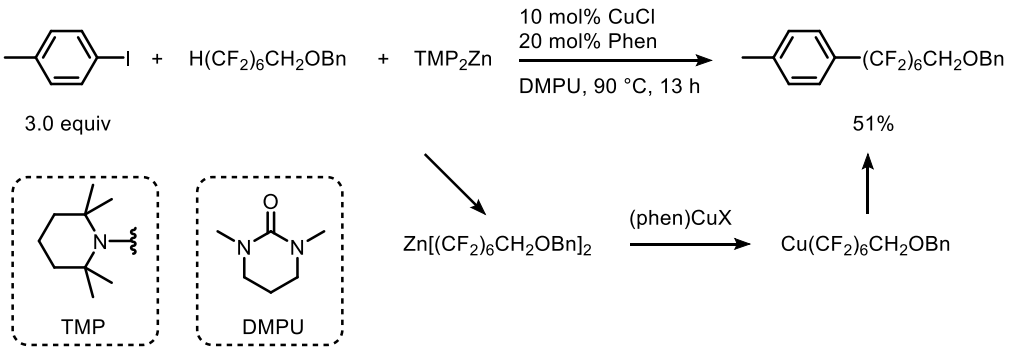


Scheme 4.3. The first structually-defined $[CuCF_3]$ complex with NHC ligand.[34a]



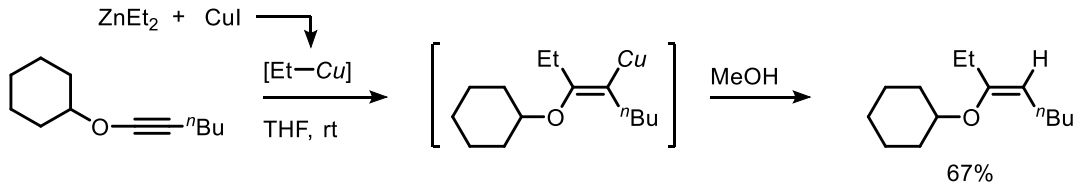
Scheme 4.4. Synthesis and reactivity of $[(phen)CuCF_3]$.[35a]

In addition to the methods with fluoroalkyl halide or fluoroalkyl silane, recently, a variety of Cu(I)-mediated or catalyzed fluoroalkylation reaction with fluoroalkylcopper complex $[R_FCu]$ generated in situ from $[R_FH]$ have been developed.[31g,36]

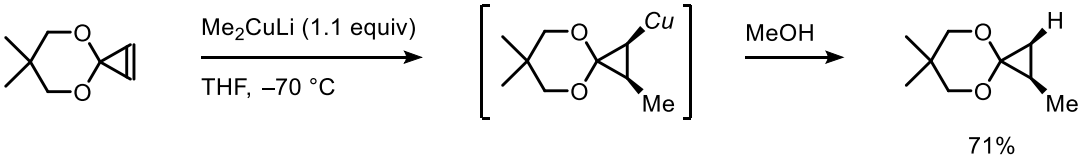


Scheme 4.5. Cu(I)-catalyzed coupling reaction with $H(CF_2)_6CH_2OBn$.[36]

As described above, it has been known that fluoroalkylcopper complexes have high reactivity toward coupling reaction with iodoarenes. Recent developments have enabled preparations of a various kinds of fluoroalkylcopper complex, and fluoroalkylation reactions with these complexes. However, to the best of our knowledge, there is no example for the preparation of fluoroalkylcopper complex by using carbocupration of fluoroalkenes, although carbocupration is one of the most reliable methods to prepare organocopper complex (Scheme 4.7).[37,38] Except for highly strained cyclopropenes,[39] alkenes are not considered to be applicable to carbocupration, but fluoroalkenes should be able to undergo carbocupration because of their high reactivity toward addition reaction as described in chapter 1. It is expected that the carbocupration of fluoroalkenes would afford a new class of fluoroalkylcopper complexes that provide an novel synthetic route to organofluorine compounds that are difficult to prepare by conventional methods.

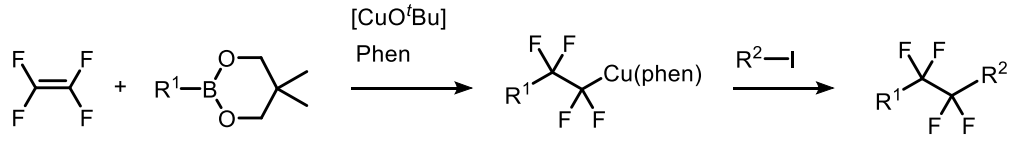


Scheme 4.6. Example of transformation via carbocupration of alkyne.[37]



Scheme 4.7. Transformation via carbocupration of cyclopropene.[39]

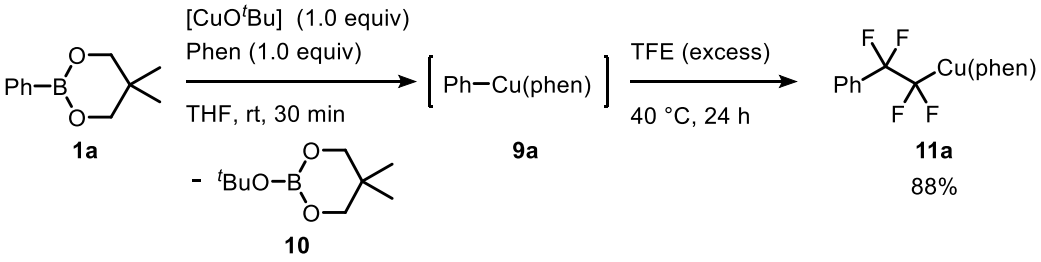
In this study, a novel synthetic method to construct tetrafluoroethylene-bridging structure by using Cu(I) complex was developed. The key synthetic intermediates are 2-aryl-1,1,2,2-tetrafluoroethylcopper complexes ligated with Phen, which are generated by carbocupration of TFE. Its structure was clearly determined by X-ray diffraction analysis. A variety of compounds bearing tetrafluoroethylene-bridging structure were prepared with the complex.



Scheme 4.8. Construction of tetrafluoroethylene-bridging structure via carbocupration of TFE.

4.2 Preparation of (phen)$CuCF_2CF_2Ph$ by the carbocupration of TFE

The carbocupration of TFE proceeded with [CuO^tBu], Phen, and arylboronates **1** as aryl transfer reagents (Scheme 4.9). First, a phenylcopper complex [(phen)CuPh] (**9a**) was prepared by the reaction of 5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane (**1a**), [CuO^tBu], and Phen in THF.[40] The reaction was completed within 10 min at room temperature, and the quantitative formation of **9a** and **10** was confirmed by ^1H and ^{11}B NMR analysis. Then, the THF solution including **9a** and **10** was exposed to TFE (3.5 atm) and heated at 40 °C for 24 h. After the removal of TFE and THF under reduced pressure, the resultant solid was washed with ether to give [(phen)$CuCF_2CF_2Ph$] (**11a**) in 88% yield as a brown solid. This is the first example of the preparation of a fluoroalkylcopper complex via carbocupration of a fluoroalkene.[41] It is worth noting that **11a** was stable under N_2 at room temperature and could be stored for at least a few months without decomposition.



Scheme 4.9. Preparation of **11a** by the carbocupration of **9a** with TFE.

Although organoboron compounds are less common in the preparation of organocopper reagents,[42] their use confers great advantages with regard to ease of handling and functional group tolerance. Furthermore, the weak Lewis acidic nature of both **1** and **10** is quite important for the synthesis of **11** because Lewis acidic species can cause decomposition of the complex through α- or β-fluorine elimination. In fact, the reaction using PhMgBr instead of **1a** did not produce **11a** at all, and trifluorostyrene (**2a**) was obtained in 70% yield as a result of β-fluorine elimination. Moreover, **11a** was found to be immediately converted into **2a** by treatment with $MgBr_2$ at room temperature. We assumed that the Lewis acidic metal species were involved in the β-fluorine elimination step through interaction with a fluorine atom. Although organoboron compounds also have a potential Lewis acidic nature, their Lewis acidity might be very low to avoid the β-fluorine elimination during the synthesis of **11h**.

4.3 Characterization of (phen)CuCF_2CF_2Ar

An analogous complex bearing a fluorine substituent at the 4-position, [(phen)CuCF_2CF_2(4-C_6H_4F)] (**11b**), was also prepared in 89% yield with 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane as a starting material. The molecular structure of **11b** was determined by X-ray crystallography (Figure 4.1). A single crystal suitable for X-ray diffraction analysis was obtained by recrystallization from a saturated solution of 11h in THF at room temperature. The revealed monomeric structure clearly shows the formation of Cu−C and C−C bonds. The sum of the three bond angles around the Cu atom is 359.78°. Thus, Cu, C1, N1, and N2 are in the same plane, and **11b** has a trigonal-planar molecular geometry. The −CF_2CF_2(4-C_6H_4F) group leans to one side as a result of the crystal packing, with one N−Cu−C angle larger than the other [N1−Cu−C1 = 117.43(11)°, N2−Cu−C1 = 161.65(11)°] and one N−Cu distance longer than the other [N1−Cu = 2.157(3) Å, N2−Cu = 1.981(2) Å].

As shown in Figure 4.2, NMR analysis showed that in solution **11b** exists as a mixture of a neutral form, [(phen)CuCF_2CF_2(4-C_6H_4F)] (**11b-n**), and an ionic form, [$(phen)_2$Cu][Cu(CF_2CF_2(4-C_6H_4F))$_2$] (**11b-i**). In the ^{19}F NMR spectrum of **11b** in THF-d_8, broad signals assigned to **11b-n** were observed at −110.4, −112.0 (for −CF_2CF_2−), and −120.1 ppm (for Ar−F). Those assigned to **11b-i** were observed at −115.0, −118.3, and −120.3 ppm. The **11b-n**:**11b-i** peak-area ratio was ca. 5:2 but depended on the concentration of **11b** and the polarity of the solvent. The dynamic behavior of **11b** in solution is consistent with previous studies of fluoroalkylcopper complexes.[34b,35a,43]

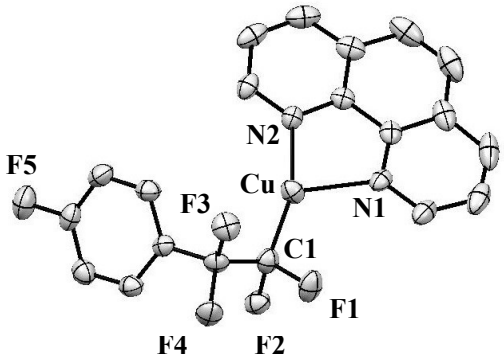


Figure 4.1. ORTEP structure of **11b**. H atoms were omitted for clarity.

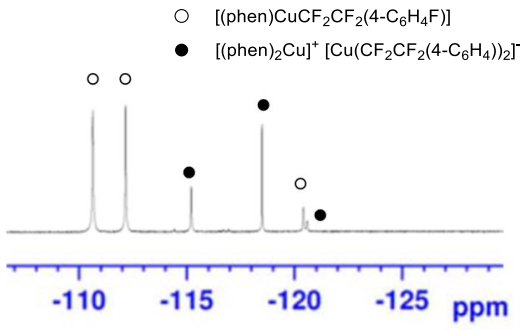
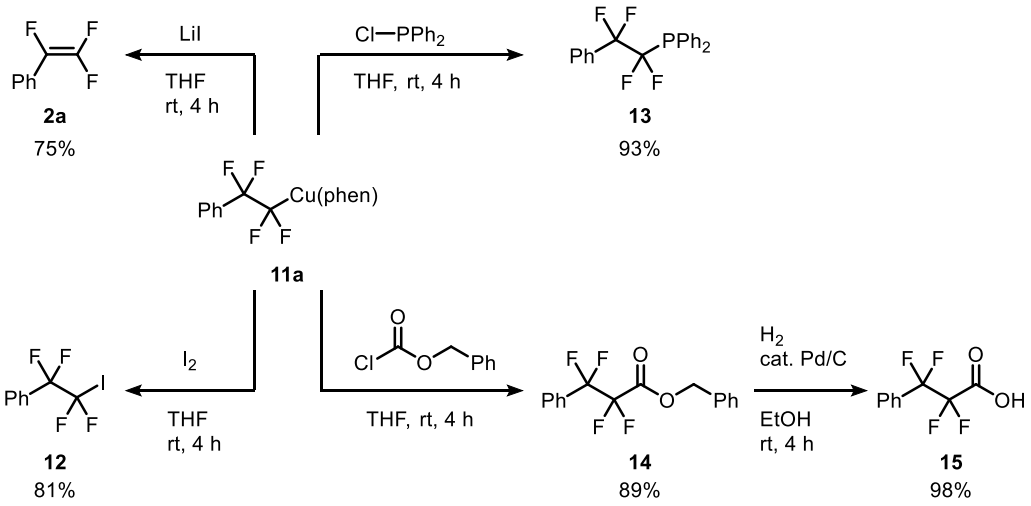


Figure 4.2. ^{19}F NMR spectrum of **11b** in THF-d_8.

4.4 Transformation reactions of (phen)CuCF_2CF_2Ph

Next, the reactivity of isolated **11a** was investigated (Scheme 4.10). As mentioned above, treatment of **11a** with $MgBr_2$ afforded **2a** via *β*-fluorine elimination. Iodonolysis of **11a** at room temperature gave (1,1,2,2-tetrafluoro-2-iodoethyl)benzene (**12**) in 81% yield. A phosphine compound bearing a fluoroalkyl group (**13**) was obtained by the reaction of **11a** with PPh_2Cl. Moreover, the reaction of **11a** with benzyl chloroformate generated a C−C bond to give the corresponding ester **14** in 89% yield, and subsequent hydrogenation catalyzed by 10% Pd/C afforded the corresponding carboxylic acid **15** quantitatively.

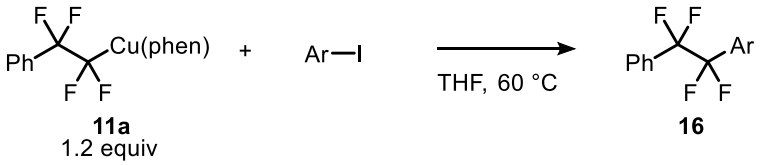


Scheme 4.10. Transformation reactions of **11a** into organofluorine compounds.

Furthermore, **11a** was also applicable for the coupling reaction with iodoarenes to give 1,2-diaryl-1,1,2,2-tetrafluoroethanes **16** (Table 4.1). After the preliminary screening of the reaction conditions, it was found that the reaction of iodobenzene with 1.2 equiv of **11a** in THF proceeded at 60 °C to afford 1,1,2,2-tetrafluoro-1,2-diphenylethane (**16a**) in 98% yield. Under the reaction conditions, electron-deficient 4-iodobenzotrifluoride reacted with **11a** smoothly to give **16b** in 97% yield. The reactions with electron-rich 4-iodoanisole and sterically-hindered iodomesitylene were sluggish, but the corresponding coupling products **16c** and **16d** were obtained in high yields. Functional groups such as formyl, ester, and cyano were tolerant of the reaction conditions (**16e-g**). Substrates bearing a C−C triple bond or a boronate, phosphate, amino, bromo, or chloro group were converted to the corresponding products (**16h−l**), which are potential substrates for further functionalization by, for example, Suzuki-Miyaura coupling or Horner-Wadsworth-Emmons reaction. In addition, 1,4-diiodobenzene was selectively

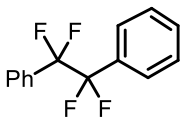
converted to either the mono- or disubstituted product depending on the stoichiometric proportions: the reaction using excess 1,4-diiodobenzene gave the monosubstituted product (**16m**) in 71% yield, and that using excess **11a** gave the disubstituted product (**16n**) in 67% yield. It was found that 2-iodopyridine and alkenyl iodide also reacted with **11a** to give the products **16o** and **16p** in excellent yields. The coupling reaction of **11a** with bromobenzene did not occur, but electron-deficient 4-bromophthalic anhydride reacted with **11a** to afford the corresponding coupling product **16q**.

Table 4.1. Coupling reaction of **11a** with iodoarenes.

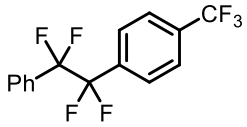


11a
1.2 equiv

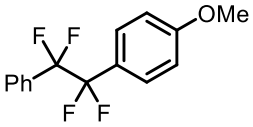
16



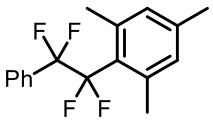
16a, 92% (4 h)



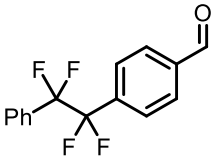
16b, 97% (4 h)



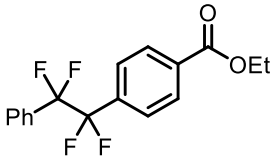
16c, 93% (24 h)



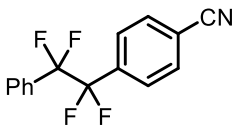
16d, 84% (48 h)



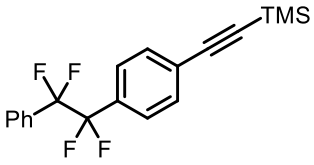
16e, 99% (4 h)



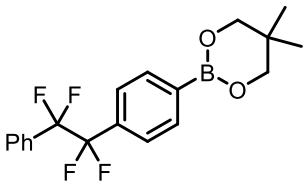
16f, 98% (4 h)



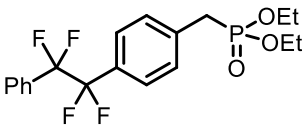
16g, 94% (4 h)



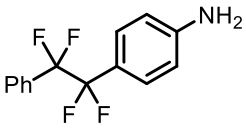
16h, 78% (12 h)



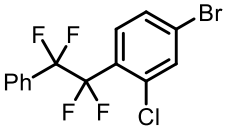
16i, 48% (12 h)



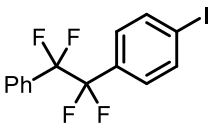
16j, 71% (12 h)



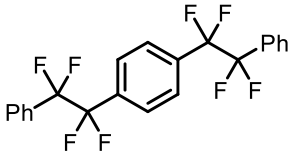
16k, 95% (20 h)



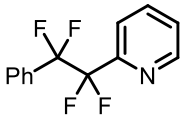
16l, 81% (12 h)



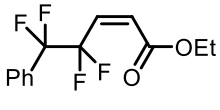
16m, 71% (12 h)[a]



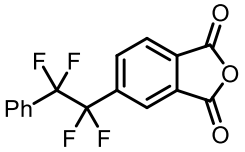
16n, 67% (4 h)[b]



16o, 97% (4 h)



16p, 91% (4 h)



16q, 63% (6 h)[c]

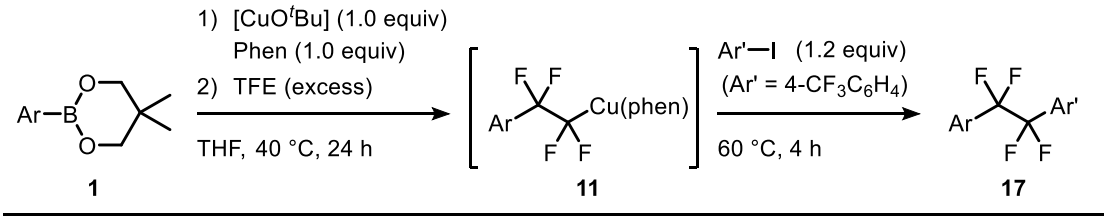
Isolated yields. (a) Conducted with excess amount of 1,4-diiodobenzene. (b) Conducted with excess amount of **11a**. (c) Conducted with corresponding bromide inatead of iodide.

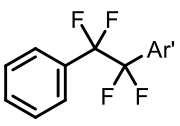
4.5 One-pot synthesis of 1,2-diaryl-1,1,2,2-tetrafluoroethanes

In addition to the above-mentioned stepwise reaction using **11a**, conducted was a one-pot synthesis of 1,2-diaryl-1,1,2,2-tetrafluoroethanes **16** from **1**, TFE, and iodoarenes without isolation of the corresponding fluoroalkylcopper complexes **11**. First, **9a** was generated in situ by the reaction of **1a**, [CuO^{t}Bu], and Phen, and the resultant solution was transferred to an autoclave reactor. TFE (3.5 atm) was charged into the reactor, and the reaction mixture was heated at 40 °C for 24 h. After the removal of TFE under reduced pressure, the reaction mixture was heated with a small excess amount of 4-iodobenzotrifluoride at 60 °C for 4 h. The target compound **17a** was isolated in 92% yield after separation by silica gel column chromatography.

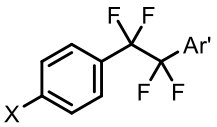
It was found that various substituted arylboronates **1** were converted into **17** (Table 4.2). Fluorine, chlorine, and bromine substituents were tolerated in the reaction (**17b-d**). The reactions using electron-rich arylboronates proceeded to give the products in high yields (**17e** and **17f**). The carbocupration reactions with electron-deficient arylboronates were relatively sluggish and required longer reaction times in order to complete the formation of **11** (**17g**−**i**). An arylboronate bearing a vinyl group was also applicable to the carbocupration of TFE (**17j**).

Table 4.2. One-pot synthesis of **17** with substituted arylboronates.

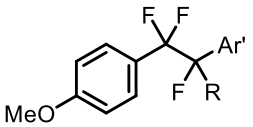




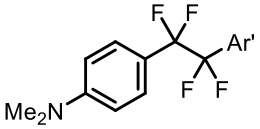
17a, 92%



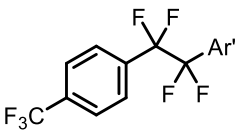
X = F **17b**, 92%
Cl **17c**, 86%
Br **17d**, 88%



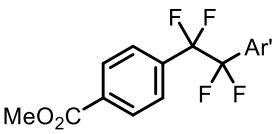
17e, 87%



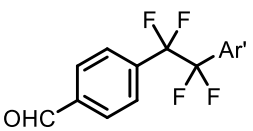
17f, 90%



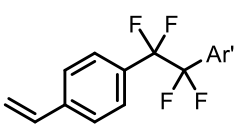
17g, 75%[a]



17h, 61%[a]



17i, 82%[a]

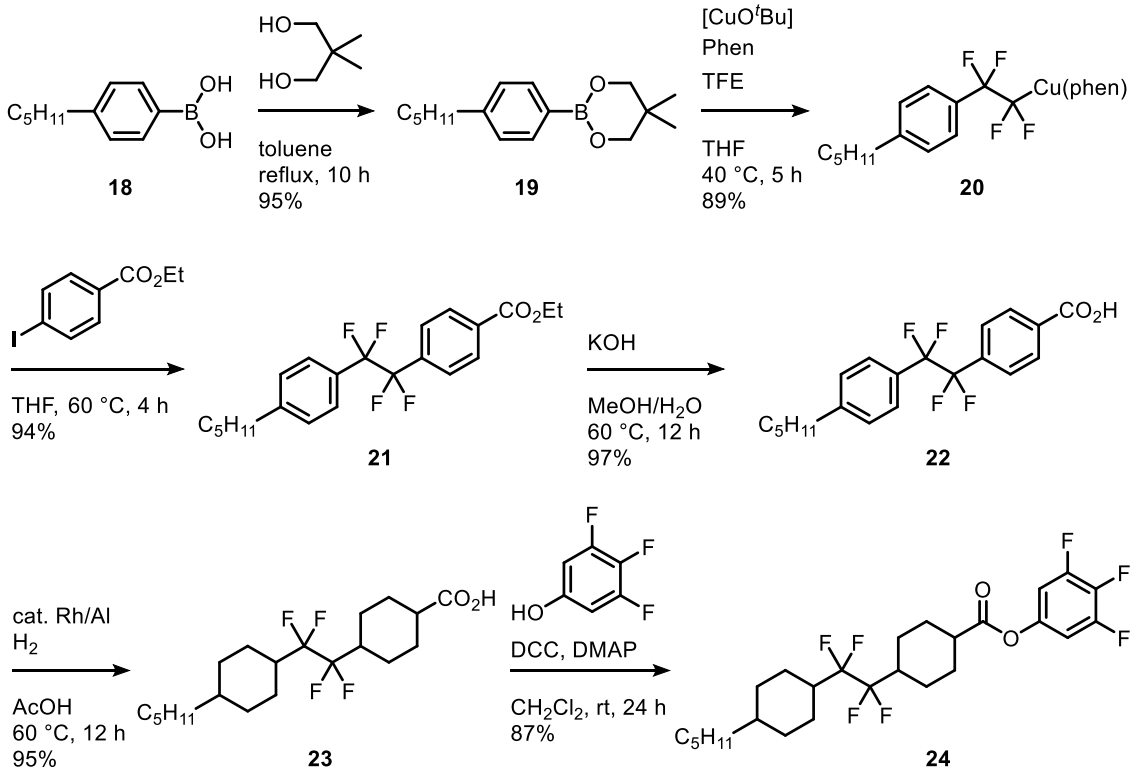


17j, 94%

Isolated yieds. a) Heated at 40 °C for 48 h before the addition of 4-iodobenzotrifluoride in order to complete the formation of the corresponding complex **11**.

4.6 Synthesis of a liquid-crystalline compound

Finally, we applied the present method to the synthesis of a liquid-crystalline compound bearing a tetrafluoroethylene-bridging structure. Materials containing the tetrafluoroethylene-bridging structure are expected to be used in the next generation of active-matrix liquid crystal displays with reduced power consumption, and the development of an efficient and convenient synthetic method has been in high demand.[44] A previous report detailed the synthesis of a liquid-crystalline compound **24** in 10 steps from 4,4'-(tetrafluoroethane-1,2-diyl)diphenol.[45] By contrast, through carbocupration of TFE, **24** was synthesized in just six steps from commercially available 4-pentylphenylboronic acid (**18**) (Scheme 4.11). Even though **24** was obtained as a mixture of geometric isomers, each of the isomers was separated by means of preparative HPLC. A fluoroalkylcopper complex **20**, which is a key intermediate in this transformation, could be prepared and stored at room temperature under N_2 in a manner similar to **11a**.



Scheme 4.11. Synthesis of a liquid-crystalline compound **24**.

4.7 Conclusion

In chapter 4, a method of compounds bearing tetrafluoroethylene-bridging structure via carbocupration of TFE is described. Novel fluoroalkylcopper complexes (phen)$CuCF_2CF_2Ar$ generated by the carbocupration of TFE were prepared and its molecular structure was determined by X-ray crystallography. With the complexes, we synthesized a variety of 1,2-difunctionalized-1,1,2,2-tetrafluoroethanes in high yields. The synthetic utility of this method was demonstrated by the short-step synthesis of a liquid-crystalline compound bearing a tetrafluoroethylene-bridging structure.

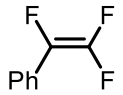
4.8 Experimental section

Preparation of [CuO^{t}Bu]: KO^{t}Bu (2.47 g, 22.0 mmol) was added to a suspension of CuI (4.19 g, 22.0 mmol) in 20 mL of THF. The mixture was stirred for 10 h at room temperature, then THF was removed under reduced pressure. On sublimation of the residue under reduced pressure at 170 °C, [CuO^{t}Bu] was obtained as a pale yellow solid (2.53 g, 84%). ^{1}H NMR (400 MHz, THF-d_8, rt, δ/ppm): 1.32 (s, 9H). $^{13}C\{^1H\}$ NMR (100.6 MHz, in C_6D_6, rt, δ/ppm): 35.7, 72.5.

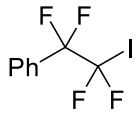
Preparation of [(phen)$CuCF_2CF_2Ph$] (11a): To a solution of [CuO^{t}Bu] (683 mg, 5.00 mmol) and 1,10-phenanthroline (Phen: 900 mg, 5.00 mmol) in THF (20 mL) was added 5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane (**1a**: 950 mg, 5.00 mmol). The resultant solution was transferred into an autoclave reactor, and then TFE (3.5 atm) was charged into the reactor. After the reaction mixture was heated at 40 °C for 24 h, all volatiles were removed under reduced pressure. The resultant solid was washed with diethyl ether for three times to give **11a** as an brown solid (1.86 g, 88%). NMR spectra of **11a** reflects the equilibrium between a neutral form [(phen)$CuCF_2CF_2Ph$] (**11a-n**) and an ionic form [$(phen)_2Cu$][$Cu(CF_2CF_2Ph)_2$] (**11a-i**). For **11a-n**, ^{1}H NMR (400 MHz, THF-d_8, rt, δ/ppm): 7.30 (br, 3H, Ph), 7.62 (br, 2H, Ph), 7.92 (br, 2H, phen), 8.05 (br, 2H, phen), 8.61 (br, 2H, phen), 9.10 (br, 2H, phen). $^{13}C\{^1H\}$ NMR (100.6 MHz, in CD_2Cl_2, rt, δ/ppm): 125.6, 127.2, 127.4 (m, Ph), 128.0 (Ph), 129.4 (Ph), 129.5, 136.4 (t, $^2J_{CF}$ = 27.8 Hz, Ph), 137.9, 144.3, 150.1. The peaks assigned to CF_2CF_2 moiety were not distinctly observed due to their multiple coupling. ^{19}F NMR (376 MHz, THF-d_8, rt, δ/ppm): –113.1 (br, 2F), –111.0 (br, 2F). For **11a-i**, ^{1}H NMR (400 MHz, THF-d_8, rt, δ/ppm): 7.20 (br, 3H, Ph), 7.52 (br, 2H, Ph), 7.92 (br, 2H, phen), 8.05 (br, 2H, phen),

8.61 (br, 2H, phen), 9.10 (br, 2H, phen). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, in CD_2Cl_2, rt, δ/ppm): 125.6, 127.2, 127.4 (m, Ph), 127.9 (Ph), 129.4 (Ph), 129.5, 136.2 (t, $^{2}J_{CF}$ = 27.8 Hz, Ph), 137.9, 144.3, 150.1. The peaks assigned to CF_2CF_2 moiety were not distinctly observed due to their multiple coupling. ^{19}F NMR (376 MHz, THF-d_8, rt, δ/ppm): –118.4 (br, 2F), –115.8 (br, 2F). Anal. Calcd for $C_{20}H_{13}CuF_4N_2$: C, 57.08; H, 3.11; N, 6.66. Found: C, 57.06; H, 3.41; N, 7.04.

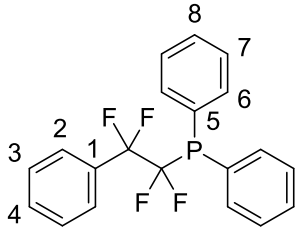
Preparation of [(phen)CuCF$_2$CF$_2$(4-C$_6$H$_4$F)] (11b): To a solution of [CuO^{t}Bu] (137 mg, 1.00 mmol) and Phen (180 mg, 1.00 mmol) in THF (5 mL) was added 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (204 mg, 1.00 mmol). The resultant solution was transferred into an autoclave reactor, and then TFE (3.5 atm) was charged into the reactor. After the reaction mixture was heated at 40 °C for 24 h, all volatiles were removed under reduced pressure. The resultant solid was washed with diethyl ether for three times to give **11b** as an brown solid (390 mg, 89%). A single crystal of **11b** suitable for X-ray diffraction analysis was obtained by recrystallization from THF at room temperature. NMR spectra of **11b** reflects the equilibrium between **11b-n** and **11b-i**. For **11b-n**, ^{1}H NMR (400 MHz, THF-d_8, rt, δ/ppm): 7.08 (dd, J_{HF} = 8.5 Hz, J_{FF} = 8.5 Hz, 2H, Ar), 7.65 (dd, J_{HF} = 8.5 Hz, J_{FF} = 5.7 Hz, 2H, Ar), 7.89 (dd, J = 8.1, 4.6 Hz, 2H, phen), 8.02 (br, 2H, phen), 8.59 (d, J = 8.1 Hz, 2H, phen), 9.00 (d, J = 4.6 Hz, 2H, phen). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, in THF-d_8, rt, δ/ppm): 114.5 (d, $^{2}J_{CF}$ = 21.8 Hz, Ar), 126.0, 127.5, 129.8, 129.9 (t, $^{3}J_{CF}$ = 6.6 Hz, Ar), 133.6 (t, $^{2}J_{CF}$ = 28.4 Hz, Ar), 138.3, 144.6, 150.6, 163.9 (d, $^{1}J_{CF}$ = 245.9 Hz, Ar). The peaks assigned to CF_2CF_2 moiety were not clearly observed due to their multiple coupling. ^{19}F NMR (376 MHz, THF-d_8, rt, δ/ppm): –120.1 (m, 1F), –112.0 (br, 2F), –110.4 (br, 2F). For **11b-i**, ^{1}H NMR (400 MHz, THF-d_8, rt, δ/ppm): 6.96 (dd, J_{HF} = 8.7 Hz, J_{FF} = 8.7 Hz, 2H, Ar), 7.52 (dd, J_{HF} = 8.7 Hz, J_{FF} = 5.6 Hz, 2H, Ar), 7.89 (dd, J = 8.1, 4.6 Hz, 2H, phen), 8.02 (br, 2H, phen), 8.59 (d, J = 8.1 Hz, 2H, phen), 9.00 (d, J = 4.6 Hz, 2H, phen). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, in THF-d_8, rt, δ/ppm): 114.4 (d, $^{2}J_{CF}$ = 21.2 Hz, Ar), 126.0, 127.5, 129.8, 130.0 (t, $^{3}J_{CF}$ = 6.9 Hz, Ar), 133.8 (t, $^{2}J_{CF}$ = 26.7 Hz, Ar), 138.3, 144.6, 150.6, 163.8 (d, $^{1}J_{CF}$ = 245.9 Hz, Ar). The peaks assigned to CF_2CF_2 moiety were not clearly observed due to their multiple coupling. ^{19}F NMR (376 MHz, THF-d_8, rt, δ/ppm): –120.3 (m, 1F), –118.3 (br, 2F), –115.0 (br, 2F). Anal. Calcd for $C_{20}H_{12}CuF_5N_2$: C, 54.74; H, 2.76; N, 6.38. Found: C, 55.49; H, 3.16; N, 6.57. X-ray data for **11b**: M = 438.87, brown, monoclinic, $P2_{1/C}$ (No,14), a = 6.9747(2) Å, b = 15.5811(3) Å, c = 15.7189(3) Å, β = 92.4420(7)°, V = 1706.68(6) Å^3, Z =4, D_{calcd} = 1.708 g/cm^3, T = –150(1) °C, R_1 (wR_2) = 0.0355 (0.0928).



Transformation of 11a into trifluorostyrene (2a): A mixture of [(phen)$CuCF_2CF_2Ph$] (**11a**: 8.4 mg, 0.02 mmol) and $MgBr_2$ (7.4 mg, 0.04 mmol) was dissolved in 0.5 mL of THF/THF-d_8 (v/v' = 4/1). The resultant solution was transferred into a J. Young NMR tube. Monitoring of the reaction by ^{19}F NMR showed that **2a** was generated in 75% yield. ^{19}F NMR (376 MHz, in THF/THF-d_8, rt, δ/ppm): –179.1 (dd, J_{FF} = 108.9, 33.2 Hz, 1F), –118.5 (dd, J_{FF} = 108.9, 73.1 Hz, 1F), –104.2 (dd, J_{FF} = 73.1, 33.2 Hz, 1F).

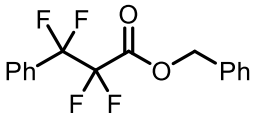


Transformation of 11a into 1,1,2,2-tetrafluoro-1-iodo-2-phenylethane (12): The reaction of [(phen)$CuCF_2CF_2Ph$] (**11a**: 126.3 mg, 0.30 mmol) with I_2 (151.8 mg, 0.60 mmol) was conducted at room temperature for 4 h. To the reaction mixture, 10.0 mL of hexane was added. Filtration of insoluble solids and the removal of the solvent under reduced pressure to give the crude product. The formation of **12** (0.242 mmol, 81%) was confirmed by NMR and MS analysis. ^1H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.44-7.51 (m, 2H), 7.53-7.61 (m, 3H). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –104.5 (t, $^3J_{FF}$ = 6.5 Hz, 2F), –58.6 (t, $^3J_{FF}$ = 6.5 Hz, 2F). MS (EI): *m/z* (%): 304 (11) [M]+, 177 (24), 127 (100), 77 (12). HRMS Calcd for $C_8H_5F_4I$ 303.9372, found *m/z* 303.9368.

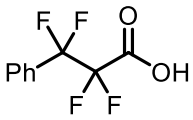


Transformation of 11a into diphenyl(1,1,2,2-tetrafluoro-2-phenylethyl)phosphine (13): The reaction of [(phen)$CuCF_2CF_2Ph$] (**11a**: 151.2 mg, 0.36 mmol) with PPh_2Cl (66.2 mg, 0.30 mmol) was conducted at room temperature for 4 h. To the reaction mixture, 10.0 mL of hexane was added. Filtration of insoluble solids and the removal of the solvent to give **13** (101.3 mg, 93%) as a colorless oil. ^1H NMR (400 MHz, in C_6D_6, rt, δ/ppm): 6.91-7.06 (m, 9H), 7.48 (d, J = 7.2 Hz, 2H), 7.68-7.76 (m, 4H). $^{13}C\{^1H\}$ NMR (100.6 MHz, in CD_2Cl_2, rt, δ/ppm): 118.3 (ttd, $^1J_{CF}$ = 253.2, $^2J_{CF}$ = 30.6, $^2J_{CP}$ =

18.5 Hz), 123.9 (tdt, $^{1}J_{CF}$ = 288.5, J_{CP} = 52.3, $^{2}J_{CF}$ = 39.7 Hz), 127.3 (t, $^{3}J_{CF}$ = 5.8 Hz, C^{2}), 128.7 (C^{3}), 129.0 (d, $^{2}J_{CP}$ = 8.3 Hz, C^{6}), 130.8 (C^{8}), 131.2 (t, $^{2}J_{CF}$ = 24.7 Hz, C^{1}), 131.6 (C^{4}) 135.6 (d, $^{3}J_{CP}$ = 22.5 Hz, C^{7}). The signal for C^{5} could not be assigned due to the overlap with other signals. ^{19}F NMR (376 MHz, in C_6D_6, rt, δ/ppm): –111.1 (dt, J_{FP} = 52.2, $^{3}J_{FF}$ = 3.5 Hz, 2F), –109.7 (dt, J_{FP} = 24.6, $^{3}J_{FF}$ = 3.5 Hz, 2F). ^{31}P{^{1}H} NMR (162 MHz, in C_6D_6, rt, δ/ppm): –2.3 (tt, J_{PF} = 52.2, 24.6 Hz). HRMS Calcd for $C_{20}H_{15}F_4P$ 362.0847, found *m/z* 326.0846.



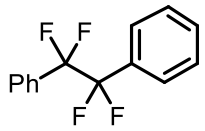
Transformation of 11a into benzyl 2,2,3,3-tetrafluoro-3-phenylpropanoate (14): The reaction of [(phen)CuCF_2CF_2Ph] (**11a**: 151.2 mg, 0.36 mmol) with benzyl chloroformate (51.2 mg, 0.30 mmol) was performed at room temperature for 4 h. The crude product was purified by flash column chromatography with hexane/ethyl acetate (v/v' = 95/5) as the eluent to give **14** (83.3 mg, 89%) as a colorless oil. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 5.34 (s, 2H), 7.34-7.47 (m, 7H), 7.49-7.58 (m, 3H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 69.0, 109.3 (tt, $^{1}J_{CF}$ = 262.4, $^{2}J_{CF}$ = 38.7 Hz), 115.5 (tt, $^{1}J_{CF}$ = 253.9, $^{2}J_{CF}$ = 31.4 Hz), 126.6 (t, $^{3}J_{CF}$ = 6.6 Hz), 128.4, 128.5, 128.7, 128.9, 129.2 (t, $^{2}J_{CF}$ = 24.2 Hz), 131.4, 133.7, 160.3 (t, $^{2}J_{CF}$ = 30.6 Hz). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –118.7 (t, J_{FF} = 5.1 Hz, 2F), –111.3 (t, J_{FF} = 5.1 Hz, 2F). HRMS Calcd for $C_{16}H_{12}F_4O_2$ 312.0773, found *m/z* 312.0771.



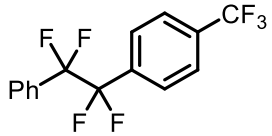
Transformation of 14 into 2,2,3,3-tetrafluoro-3-phenylpropanoic acid (15): A mixture of **14** (62.4 mg, 0.20 mmol) with a catalytic amount of 10% palladium on carbon (21.2 mg) was dissolved in 2.0 mL of ethanol. The resultant suspension was transferred into an autoclave reactor, and then H_2 (2.0 atm) was charged into the reactor. The reaction mixture was stirred at room temperature for 4 h. After the purging of H_2, the insoluble component was filtered off. All volatiles were removed under reduced pressure to afford 2,2,3,3-tetrafluoro-3-phenylpropanoic acid (**15**: 43.2 mg, 98%) as an analytically pure white solid. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.34-7.65 (m, 5H), 7.89 (br, 1H, –COO*H*). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 109.6 (br, –*C*F_2COOH), 115.6 (tt, $^{1}J_{CF}$ = 254.5, $^{2}J_{CF}$ = 31.9 Hz), 126.7 (t, $^{3}J_{CF}$ = 6.2 Hz), 128.5,

129.0 (t, $^2J_{CF}$ = 24.4 Hz), 131.7, 164.1 (br, –*C*OOH). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –118.9 (br, 2F, –C*F*$_2$COOH), –111.2 (s, 2F).

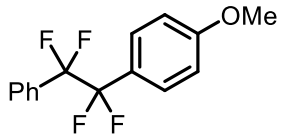
General procedure for the coupling reaction of 11a with iodoarenes (Table 4.1): To a THF solution of iodoarene, 1.2 equiv of [(phen)CuCF_2CF_2Ph] (**11a**) was added. The resultant suspension was heated at 60 °C for given time. Then, 10 mL of hexane was added to the suspension and precipitate was removed by filtration. All volatiles were removed under reduced pressure. Purification of the crude product was conducted by silica gel flash column chromatography or preparative HPLC.



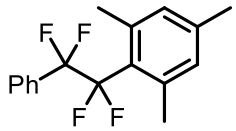
1,1,2,2-Tetrafluoro-1,2-diphenylethane (16a): Following the general procedure, the reaction with iodobenzene (20.4 mg, 0.10 mmol) was conducted for 4 h to give the title compound as a white solid (23.4 mg, 92%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 99/1) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.37-7.57 (m, 10H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 116.6 (tt, $^1J_{CF}$ = 253.1, $^2J_{CF}$ = 36.5 Hz), 126.9 (tt, J_{CF} = 3.7, 3.7 Hz), 128.0, 130.9 (t, $^2J_{CF}$ = 26.4). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –111.8 (s, 4F). HRMS Calcd for $C_{14}H_{10}F_4$ 254.0719, found *m/z* 254.0718.



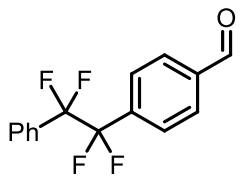
1-Trifluoromethyl-4-(1,1,2,2-tetrafluoro-2-phenylethyl)benzene (16b): Following the general procedure, the reaction with 4-iodobenzotrifluoride (27.2 mg, 0.10 mmol) was conducted for 4 h to give the title compound as a white solid (31.2 mg, 97%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 99/1) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.41-7.56 (m, 5H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.70 (d, *J* = 8.3 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 116.0 (tt, $^1J_{CF}$ = 253.2, $^2J_{CF}$ = 36.0 Hz), 116.4 (tt, $^1J_{CF}$ = 253.2, $^2J_{CF}$ = 36.0 Hz), 123.4 (q, $^1J_{CF}$ = 273.5 Hz, –*C*F$_3$), 125.1 (q, $^3J_{CF}$ = 3.6 Hz), 126.9 (t, $^3J_{CF}$ = 6.3 Hz), 127.6 (t, $^3J_{CF}$ = 6.3 Hz), 128.2, 130.3 (t, $^2J_{CF}$ = 24.4 Hz), 131.2, 133.1 (q, $^2J_{CF}$ = 32.1 Hz), 134.6 (t, $^2J_{CF}$ = 24.4 Hz). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.0 (s, 2F), –111.5 (s, 2F), –63.1 (s, 3F). HRMS Calcd for $C_{15}H_9F_7$ 322.0592, found *m/z* 322.0594.



4-(1,1,2,2-Tetrafluoro-2-phenylethyl)anisole (16c): Following the general procedure, the reaction with 4-iodoanisole (70.2 mg, 0.30 mmol) was conducted for 24 h to give the title compound as a white solid (79.0 mg, 93%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 99/1) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 3.84 (s, 3H), *6*.91 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.7 Hz, 2H), 7.38-7.52 (m, 5H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 55.3, 113.4, 116.6 (tt, $^{1}J_{CF}$ = 252.5, $^{2}J_{CF}$ = 36.7 Hz), 116.8 (tt, $^{1}J_{CF}$ = 252.5, $^{2}J_{CF}$ = 36.7 Hz), 122.9 (t, $^{2}J_{CF}$ = 25.5 Hz), 126.9 (t, $^{3}J_{CF}$ = 6.6 Hz), 128.0, 128.4 (t, $^{3}J_{CF}$ = 6.6 Hz), 130.8, 131.0 (t, $^{2}J_{CF}$ = 25.6 Hz), 161.5. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –111.9 (s, 2F), –110.8 (s, 2F). HRMS Calcd for $C_{15}H_{12}F_4O$ 284.0824, found *m/z* 284.0826.

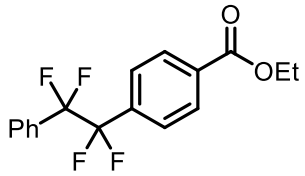


2-(1,1,2,2-Tetrafluoro-2-phenylethyl)mesitylene (16d): Following the general procedure, the reaction with 2-iodomesitylene (73.8 mg, 0.30 mmol) was conducted for 48 h to give the title compound as a white solid (74.7 mg, 84%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 99/1) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 2.33 (s, 3H), 2.39 (t, J_{HF} = 4.2 Hz, 6H), 6.93 (s, 2H), 7.44-7.51 (m, 2H), 7.52-7.60 (m, 3H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 20.7 (s, *p*-*C*H$_3$), 22.1 (m, *o*-*C*H$_3$), 118.0 (tt, $^{1}J_{CF}$ = 253.3, $^{2}J_{CF}$ = 38.1 Hz), 119.6 (tt, $^{1}J_{CF}$ = 255.8, $^{2}J_{CF}$ = 38.4 Hz), 124.3 (t, $^{2}J_{CF}$ = 21.8 Hz), 127.0 (t, $^{3}J_{CF}$ = 6.3 Hz), 128.0, 130.8, 131.3, 131.3 (t, $^{2}J_{CF}$ = 25.3 Hz), 139.2 (t, $^{3}J_{CF}$ = 3.1 Hz), 140.1. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –110.4 (s, 2F), –99.6 (s, 2F). HRMS Calcd for $C_{17}H_{16}F_4$ 296.1188, found *m/z* 296.1189.

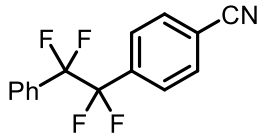


4-(1,1,2,2-Tetrafluoro-2-phenylethyl)benzaldehyde (16e): Following the general procedure, the reaction with 4-iodobenzaldehyde (69.6 mg, 0.30 mmol) was conducted for 4 h to give the title compound as a white solid (84.0 mg, 99%). Purification was

conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 95/5) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.40-7.55 (m, 5H), 7.65 (d, J = 8.3 Hz, 2H), 7.94 (d, J = 8.3 Hz, 2H), 10.09 (s, 1H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 116.1 (tt, $^{1}J_{CF}$ = 253.2, $^{2}J_{CF}$ = 36.7 Hz), 116.4 (tt, $^{1}J_{CF}$ = 253.2, $^{2}J_{CF}$ = 35.5 Hz), 126.8 (t, $^{3}J_{CF}$ = 6.5 Hz), 127.8 (t, $^{3}J_{CF}$ = 6.2 Hz), 128.2, 129.2, 130.2 (t, $^{2}J_{CF}$ = 24.8 Hz), 131.1, 136.4 (t, $^{2}J_{CF}$ = 24.9 Hz), 137.9, 191.4. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.2 (s, 2F), –111.5 (s, 2F). HRMS Calcd for $C_{15}H_{10}F_4O$ 282.0668, found *m/z* 282.0668.

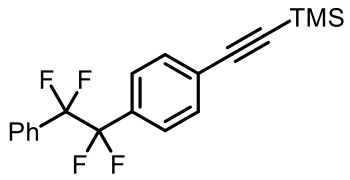


1-Ethoxycarbonyl-4-(1,1,2,2-tetrafluoro-2-phenylethyl)benzene (16f): Following the general procedure, the reaction with 4-ethoxycarbonyl-1-iodobenzene (32.6 mg, 0.10 mmol) was conducted for 4 h to give the title compound as a white solid (31.9 mg, 98%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 95/5) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 1.41 (t, J = 7.2 Hz, 3H), 4.41 (q, J = 7.2 Hz, 2H), 7.37-7.51 (m, 5H), 7.53 (d, J = 8.2 Hz, 2H), 8.08 (d, J = 8.2 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 14.2, 61.3, 116.3 (tt, $^{1}J_{CF}$ = 252.4, $^{2}J_{CF}$ = 36.5 Hz), 116.4 (tdd, $^{1}J_{CF}$ = 254.0, $^{2}J_{CF}$ = 38.2, 32.7 Hz), 126.8 (t, $^{3}J_{CF}$ = 6.2 Hz), 127.0 (t, $^{3}J_{CF}$ = 6.2 Hz), 128.1, 129.2, 130.4 (t, $^{2}J_{CF}$ = 25.0 Hz), 131.0, 132.9, 135.0 (t, $^{2}J_{CF}$ = 25.0 Hz), 165.6. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.2 (s, 2F), –111.7 (s, 2F). HRMS Calcd for $C_{17}H_{14}F_4O_2$ 326.0930 found *m/z* 326.0929.

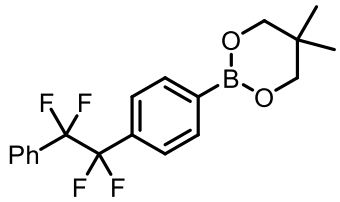


4-(1,1,2,2-Tetrafluoro-2-phenylethyl)benzonitrile (16g): Following the general procedure, the reaction with 4-iodobenzonitrile (68.7 mg, 0.30 mmol) was conducted for 4 h to give the title compound as a white solid (78.6 mg, 94%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 95/5) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.40-7.56 (m, 5H), 7.60 (d, J = 8.3 Hz, 2H), 7.72 (d, J = 8.3 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 115.1, 115.7 (tt, $^{1}J_{CF}$ = 254.9, $^{2}J_{CF}$ = 37.3 Hz), 116.3 (tt, $^{1}J_{CF}$ = 252.9, $^{2}J_{CF}$ = 35.3 Hz),

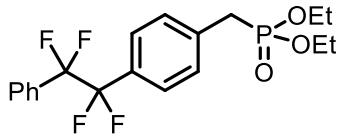
117.8, 126.8 (t, $^{3}J_{CF}$ = 6.6 Hz), 127.8 (t, $^{3}J_{CF}$ = 6.6 Hz), 128.3, 129.9 (t, $^{2}J_{CF}$ = 24.8 Hz), 131.3, 131.9, 135.3 (t, $^{2}J_{CF}$ = 25.6 Hz). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.5 (s, 2F), –112.4 (s, 2F). HRMS Calcd for $C_{15}H_9F_4N$ 279.0671, found *m/z* 279.0670.



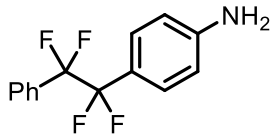
1-(4-(1,1,2,2-Tetrafluoroethyl-2-phenyl)-2-(trimethylsilyl)acetylene (16h): Following the general procedure, the reaction with 1-(4-iodophenyl)-2-trimethylsilylacetylene (90.0 mg, 0.30 mmol) was conducted for 12 h to give the title compound as a white solid (82.1 mg, 78%). Purification was conducted by preparative HPLC with $CHCl_3$. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 0.27 (s, 9H), 7.33-7.53 (m, 9H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 0.2, 96.6, 103.8, 116.4 (tt, $^{1}J_{CF}$ = 253.6, $^{2}J_{CF}$ = 35.1 Hz), 116.5 (tt, $^{1}J_{CF}$ = 253.0, $^{2}J_{CF}$ = 35.7 Hz), 125.9, 126.8 (t, $^{3}J_{CF}$ = 6.1 Hz), 126.9 (t, $^{3}J_{CF}$ = 6.1 Hz), 128.1, 130.6 (t, $^{2}J_{CF}$ = 24.8 Hz), 130.6 (t, $^{2}J_{CF}$ = 24.8 Hz), 130.9, 131.5. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.4 (s, 2F), –112.0 (s, 2F). HRMS Calcd for $C_{19}H_{18}F_4Si$ 350.1114, found *m/z* 350.1112.



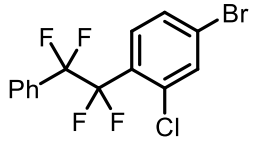
2-(4-(1,1,2,2-Tetrafluoro-2-phenylethyl))-5,5-dimethyl-1,3,2-dioxaborinane (16i): Following the general procedure, the reaction with 2-(4-iodophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (94.8 mg, 0.30 mmol) was conducted for 12 h to give the title compound as a white solid (52.3 mg, 48%). Purification was conducted by preparative HPLC with $CHCl_3$. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 1.03 (s, 6H), 3.78 (s, 4H), 7.37-7.51 (m, 7H), 7.83 (d, *J* = 8.1 Hz, 2H). ^{11}B NMR (128 MHz, in $CDCl_3$, rt, δ/ppm): 26.5 (br). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 21.8, 31.8, 72.3, 116.6 (tt, $^{1}J_{CF}$ = 253.1, $^{2}J_{CF}$ = 35.9 Hz), 116.7 (tt, $^{1}J_{CF}$ = 254.2, $^{2}J_{CF}$ = 36.9 Hz), 125.9 (t, $^{3}J_{CF}$ = 6.2 Hz), 126.9 (t, $^{3}J_{CF}$ = 6.2 Hz), 128.0, 130.8, 130.8 (t, $^{2}J_{CF}$ = 24.7 Hz), 132.7 (t, $^{2}J_{CF}$ = 24.4 Hz), 133.4. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.2 (s, 2F), –111.9 (s, 2F). HRMS Calcd for $C_{19}H_{19}F_4O_2B$ 366.1414, found *m/z* 366.1412.



Diethyl (4-(1,1,2,2-tetrafluoro-2-phenylethyl))benzyl)phosphonate (16j): Following the general procedure, the reaction with diethyl (4-iodobenzyl)phosphonate (106.2 mg, 0.30 mmol) was conducted for 12 h to give the title compound as a white solid (86.1 mg, 71%). Purification was conducted by preparative HPLC with $CHCl_3$. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 1.23 (t, J = 7.0 Hz, 6H), 3.17 (d, J = 22.0 Hz, 2H), 3.96-4.05 (m, 4H), 7.32-7.49 (m, 9H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 16.3 (d, J = 5.9 Hz), 33.6 (d, J_{CP} = 137.9 Hz), 62.2 (d, J_{CP} = 6.8 Hz), 116.5 (tt, $^1J_{CF}$ = 253.0, $^2J_{CF}$ = 36.0 Hz), 116.5 (tt, $^1J_{CF}$ = 253.0, $^2J_{CF}$ = 36.0 Hz), 126.8 (t, $^3J_{CF}$ = 6.3 Hz), 127.1 (br), 128.0, 129.4 (td, $^2J_{CF}$ = 25.1 Hz, J = 3.7 Hz), 129.4 (d, J= 6.5 Hz), 130.7 (t, $^2J_{CF}$ = 24.8 Hz), 130.8, 135.0 (d, J = 9.1 Hz). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –111.8 (s, 2F), –111.7 (s, 2F). ^{31}P{^{1}H} NMR (162 MHz, in $CDCl_3$, rt, δ/ppm): 25.4 (br). HRMS Calcd for $C_{19}H_{21}F_4O_3P$ 404.1164, found *m/z* 404.1159.

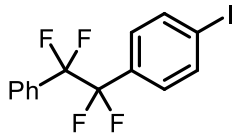


4-(1,1,2,2-Tetrafluoro-2-phenylethyl)aniline (16k): Following the general procedure, the reaction with 4-iodoaniline (65.7 mg, 0.30 mmol) was conducted for 20 h to give the title compound as a white solid (76.6 mg, 95%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 95/5) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 3.86 (br, 2H, NH_2), 6.64 (d, J = 8.3, 2H), 7.20 (d, J = 8.3 Hz, 2H), 7.37-7.52 (m, 5H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 113.9, 116.7 (tt, $^1J_{CF}$ = 252.9, $^2J_{CF}$ = 37.1 Hz), 116.5 (tt, $^1J_{CF}$ = 252.3, $^2J_{CF}$ = 35.8 Hz), 120.2 (t, $^2J_{CF}$ = 25.7 Hz), 126.9 (t, $^3J_{CF}$ = 6.3 Hz), 127.9, 128.2 (t, $^3J_{CF}$ = 6.4 Hz), 130.6, 131.2 (t, $^2J_{CF}$ = 25.0Hz), 148.6. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.0 (s, 2F), –110.7 (s, 2F). HRMS Calcd for $C_{14}H_{11}F_4N$ 269.0828, found *m/z* 269.0825.

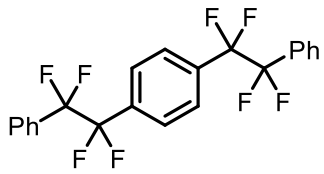


4-Bromo-2-chloro-1-(1,1,2,2-tetrafluoro-2-phenylethyl)benzene (16l): Following the general procedure, the reaction with 4-bromo-2-chloro-1-iodobenzene (95.2 mg, 0.30

mmol) was conducted for 12 h to give the title compound as a white solid (89.1 mg, 81%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 99/1) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.38 (d, J = 8.4 Hz, 1H), 7.41-7.54 (m, 6H), 7.64 (m, 1H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 116.2 (tt, $^{1}J_{CF}$ = 256.0, $^{2}J_{CF}$ = 38.6 Hz), 116.8 (tt, $^{1}J_{CF}$ = 253.9, $^{2}J_{CF}$ = 36.4 Hz), 125.8, 127.0 (t, $^{3}J_{CF}$ = 6.9 Hz), 127.5 (t, $^{2}J_{CF}$ = 24.4 Hz), 128.2, 129.7, 130.3 (t, $^{2}J_{CF}$ = 24.6 Hz), 131.1, 131.4 (t, $^{3}J_{CF}$ = 8.5 Hz), 134.3, 134.5 (t, $^{3}J_{CF}$ = 2.7 Hz). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –110.4 (t, J_{FF} = 9.6 Hz, 2F), –107.6 (t, J_{FF} = 9.6 Hz, 2F), –65.4 (s, 3F). HRMS Calcd for $C_{14}H_8BrClF_4$ 365.9434, found *m/z* 365.9438.

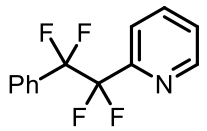


4-(1,1,2,2-Tetrafluoro-2-phenylethyl)iodobenzene (16m): The reaction of (phen)$CuCF_2CF_2Ph$ (**11a**: 126.3 mg, 0.30 mmol) with 1,4-diiodobenzene (494.8 mg, 1.50 mmol) was conducted at 60 °C for 12 h. The crude product was purified by preparative HPLC with $CHCl_3$ to give the title compound as a white solid (81.1 mg, 71%). 347.2 mg of unreacted 1,4-diiodobenzene was recovered as an analytically pure solid. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.19 (d, J = 8.0 Hz, 2H), 7.39-7.55 (m, 5H), 7.78 (d, J = 8.0 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 97.8, 116.3 (tt, $^{1}J_{CF}$ = 253.4, $^{2}J_{CF}$ = 36.6 Hz), 116.4 (tt, $^{1}J_{CF}$ = 253.4, $^{2}J_{CF}$ = 36.6 Hz), 126.8 (t, $^{3}J_{CF}$ = 6.3 Hz), 128.1, 128.6 (t, $^{3}J_{CF}$ = 6.3 Hz), 130.4 (t, $^{2}J_{CF}$ = 24.4 Hz), 130.5 (t, $^{2}J_{CF}$ = 24.4 Hz), 131.0, 137.3. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.1 (s, 2F), –111.7 (s, 2F). HRMS Calcd for $C_{14}H_9F_4I$ 379.9685, found *m/z* 379.9683.

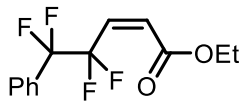


Bis(1,1,2,2-tetrafluoro-2-phenylethyl)benzene (16n): The reaction of (phen)$CuCF_2CF_2Ph$ (**11a**: 303.0 mg, 0.72 mmol) with 1,4-diiodobenzene (99.0 mg, 0.30 mmol) was conducted at 60 °C for 4 h. The crude product was purified by preparative HPLC with $CHCl_3$ to give the title compound as a white solid (86.4 mg, 67%). ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.42-7.53 (m, 14H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 116.2 (tt, $^{1}J_{CF}$ = 253.7, $^{2}J_{CF}$ = 36.0 Hz), 116.4 (tt, $^{1}J_{CF}$ = 253.7, $^{2}J_{CF}$ = 5.4 Hz), 126.9 (t, $^{3}J_{CF}$ = 6.1 Hz), 126.9 (t, $^{3}J_{CF}$ = 6.1 Hz), 128.2, 130.4 (t, $^{2}J_{CF}$ = 24.8

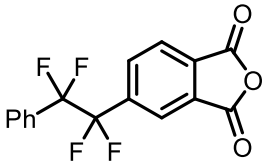
Hz), 131.1, 133.6 (t, $^{2}J_{CF}$ = 25.8 Hz). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.1 (s, 2F), –111.7 (s, 2F). HRMS Calcd for $C_{22}H_{14}F_8$ 430.0968, found *m/z* 430.0970.



2-(1,1,2,2-Tetrafluoro-2-phenylethyl)pyridine (16o): Following the general procedure, the reaction with 2-iodopyridine (61.5 mg, 0.30 mmol) was conducted for 4 h to give the title compound as a white solid (74.1 mg, 97%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 95/5) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.39-7.56 (m, 6H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.82 (t, *J* = 7.8 Hz, 1H), 8.71 (d, *J* = 4.2 Hz, 1H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 114.2 (tt, $^{1}J_{CF}$ = 252.8, $^{2}J_{CF}$ = 37.2 Hz), 116.5 (tt, $^{1}J_{CF}$ = 254.0 $^{2}J_{CF}$ = 34.9 Hz), 122.6 (t, $^{3}J_{CF}$ = 4.4 Hz), 125.4, 126.8 (t, $^{3}J_{CF}$ = 6.4 Hz), 128.2, 130.6 (t, $^{2}J_{CF}$ = 25.2 Hz), 131.0, 136.7, 149.4, 149.6 (t, $^{2}J_{CF}$ = 26.2 Hz). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –114.7 (t, *J* = 6.5 Hz, 2F), –111.1 (t, *J* = 6.5 Hz, 2F). HRMS Calcd for $C_{13}H_9F_4N$ 255.0671, found *m/z* 255.0666.

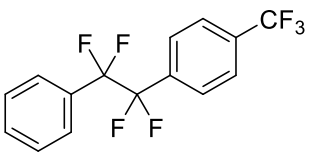


Ethyl (*Z*)-4,4,5,5-tetrafluoro-5-phenylpent-2-enoate (16p): Following the general procedure, the reaction with *cis*-3-iodo-acrylate (73.8 mg, 0.30 mmol) was conducted for 4 h to give the title compound as a colorless oil (75.4 mg, 91%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 95/5) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 1.28 (t, *J* = 7.1 Hz, 3H), 4.21 (q, *J* = 7.1 Hz, 2H), 6.02 (dtt, J_{HF} = 13.7, J_{HH} = 13.1, J_{HF} = 1.1 Hz, 1H), 6.35 (dt, J_{HH} = 13.1, J_{HF} = 2.3), 7.43-7.60 (m, 5H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 13.8, 61.3, 114.3 (tt, $^{1}J_{CF}$ = 251.0, $^{2}J_{CF}$ = 38.3 Hz), 116.2 (tt, $^{1}J_{CF}$ = 252.9, $^{2}J_{CF}$ = 38.3 Hz), 124.8 (t, $^{2}J_{CF}$ = 25.3 Hz), 126.8 (t, $^{3}J_{CF}$ = 6.2 Hz), 128.2, 130.0 (t, $^{2}J_{CF}$ = 24.6 Hz), 130.2 (t, $^{3}J_{CF}$ = 5.9 Hz), 131.1, 164.6. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –111.6 (s, 2F), –110.9 (d, J_{HF} = 13.7, 2F). HRMS Calcd for $C_{13}H_{12}F_4O_2$ 276.0773, found *m/z* 276.0773.

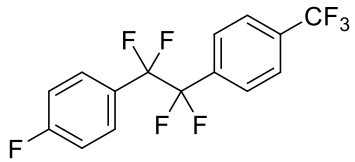


4-(1,1,2,2-Tetrafluoro-2-phenylethyl)phthalic anhydride (16q): Following the general procedure, the reaction with 4-bromophthalic anhydride (68.1 mg, 0.30 mmol) was conducted for 6 h to give the title compound as a white solid (61.1 mg, 63%). Purification was conducted by preparative HPLC. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.45-7.59 (m, 5H), 8.05 (d, J = 7.9 Hz, 1H), 8.11 (d, J = 7.9 Hz, 1H), 8.18 (s, 1H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 115.5 (tt, $^{1}J_{CF}$ = 254.5, $^{2}J_{CF}$ = 37.4 Hz), 116.2 (tt, $^{1}J_{CF}$ = 253.4, $^{2}J_{CF}$ = 35.0 Hz), 124.7 (t, $^{3}J_{CF}$ = 6.5 Hz), 125.6, 126.8 (t, $^{3}J_{CF}$ = 6.3 Hz), 128.5, 129.4 (t, $^{2}J_{CF}$ = 24.6 Hz), 131.4, 131.6, 133.3, 134.7 (t, $^{3}J_{CF}$ = 5.5 Hz), 139.3 (t, $^{2}J_{CF}$ = 25.8 Hz), 161.5, 161.6. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –111.3 (s, 2F), –110.7 (s, 2F). HRMS Calcd for $C_{16}H_8F_4O_3$ 324.0410, found *m/z* 324.0409.

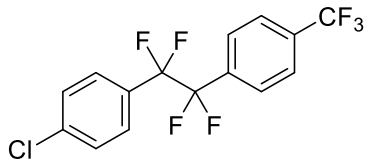
General procedure for the one-pot synthesis of compounds bearing tetrafluoroethylene-bridging structure (Table 4.2): To a solution of [CuO^{t}Bu] (41.0 mg, 0.30 mmol) and Phen (54.0 mg, 0.30 mmol) in THF (5 mL) was added arylboronate (**1**: 0.30 mmol). The resultant solution was transferred into an autoclave reactor, and then TFE (3.5 atm) was charged into the reactor. The reaction mixture was heated at 40 °C for 24 h (or 48 h). After the removal of TFE under reduced pressure, 4-iodobenzotrifluoride (97.9 mg, 0.36 mmol) was added, then the resultant solution was heated at 60 °C for 4 h. All volatiles were removed under reduced pressure. Purification of the crude product was conducted by flash column chromatography.



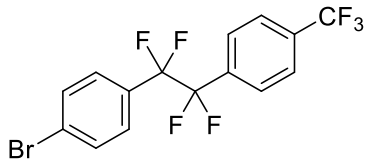
4-(1,1,2,2-Tetrafluoro-2-phenylethyl)benzotrifluoride (17a): Following the general procedure, the reaction with 5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane (**1a**: 57.0 mg, 0.30 mmol) was conducted to give the title compound as a white solid (88.9 mg, 92%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 99/1) as the eluent.



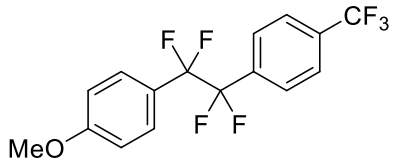
4-(1,1,2,2-Tetrafluoro-2-(4-fluorophenyl)ethyl)benzotrifluoride (17b): Following the general procedure, the reaction with 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (62.4 mg, 0.30 mmol) was conducted to give the title compound as a white solid (94.0 mg, 92%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 99/1) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.14 (dd, J = 8.3, 8.7 Hz, 2H), 7.49 (dd, J = 5.3, 8.7 Hz, 2H), 7.62 (d, J = 8.5 Hz, 2H), 7.72 (d, J = 8.5 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 115.5 (d, $^{2}J_{CF}$ = 22.5 Hz), 115.9 (tt, $^{1}J_{CF}$ = 253.2, $^{2}J_{CF}$ = 37.2 Hz), 116.2 (tt, $^{1}J_{CF}$ = 253.2, $^{2}J_{CF}$ = 36.6 Hz), 123.4 (q, $^{1}J_{CF}$ = 272.4 Hz, –*C*F$_3$), 125.2 (q, $^{3}J_{CF}$ = 3.8 Hz), 126.2 (td, $^{2}J_{CF}$ = 25.2 Hz, $^{3}J_{CF}$ = 3.1 Hz), 127.6 (t, $^{3}J_{CF}$ = 6.4 Hz), 128.4 (dt, $^{2}J_{CF}$ = 8.4 Hz, $^{3}J_{CF}$ = 6.6 Hz), 133.2 (q, $^{2}J_{CF}$ = 32.6 Hz), 134.3 (t, $^{2}J_{CF}$ = 25.2 Hz), 164.4 (d, $^{1}J_{CF}$ = 251.4 Hz). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –111.9 (s, 2F), –110.7 (s, 2F). –108.6 (m, 1F, –C$_6$H$_4$*F*), –63.0 (s, 3F). HRMS Calcd for $C_{15}H_8F_8$ 340.0498, found *m/z* 340.0500.



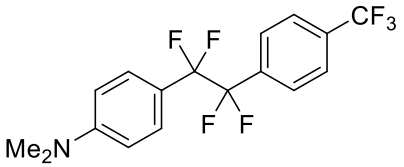
4-(1,1,2,2-Tetrafluoro-2-(4-chlorophenyl)ethyl)benzotrifluoride (17c): Following the general procedure, the reaction with 2-(4-chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (67.3 mg, 0.30 mmol) was conducted to give the title compound as a white solid (91.9 mg, 86%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 99/1) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.43 (s, 4H), 7.62 (d, J = 7.8 Hz, 2H), 7.72 (d, J = 7.8 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 115.9 (tt, $^{1}J_{CF}$ = 252.8, $^{2}J_{CF}$ = 37.3 Hz), 116.1 (tt, $^{1}J_{CF}$ = 251.2, $^{2}J_{CF}$ = 36.8 Hz), 123.5 (q, $^{1}J_{CF}$ = 272.0 Hz, –*C*F$_3$), 125.3 (q, $^{3}J_{CF}$ = 3.5 Hz), 127.6 (t, $^{3}J_{CF}$ = 6.3 Hz), 128.4 (t, $^{3}J_{CF}$ = 6.5 Hz), 128.6, 128.7 (t, $^{2}J_{CF}$ = 25.3 Hz), 133.2 (q, $^{2}J_{CF}$ = 33.0 Hz), 134.2 (t, $^{2}J_{CF}$ = 25.2 Hz), 137.7. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –111.8 (s, 2F), –111.3 (s, 2F), –63.0 (s, 3F). HRMS Calcd for $C_{15}H_8F_7Cl$ 356.0203, found *m/z* 356.0205.



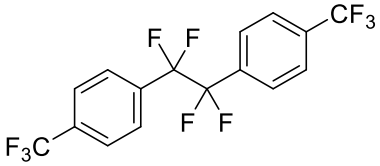
4-(1,1,2,2-Tetrafluoro-2-(4-bromophenyl)ethyl)benzotrifluoride (17d): Following the general procedure, the reaction with 2-(4-bromophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (81.3 mg, 0.30 mmol) was conducted to give the title compound as a white solid (105.6 mg, 88%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 99/1) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.37 (d, J = 8.5 Hz, 2H), 7.60 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 8.5 Hz, 2H), 7.72 (d, J = 8.5 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 115.8 (tt, $^{1}J_{CF}$ = 253.0, $^{2}J_{CF}$ = 36.2 Hz), 116.2 (tt, $^{1}J_{CF}$ = 253.7, $^{2}J_{CF}$ = 36.7 Hz), 123.5 (q, $^{1}J_{CF}$ = 273.6 Hz, –CF$_3$), 125.3 (q, $^{3}J_{CF}$ = 3.8 Hz), 126.1, 127.6 (t, $^{3}J_{CF}$ = 6.3 Hz), 128.6 (t, $^{3}J_{CF}$ = 6.3 Hz), 129.3 (t, $^{2}J_{CF}$ = 25.2 Hz), 131.6, 133.3 (q, $^{2}J_{CF}$ = 32.8 Hz), 134.1 (t, $^{2}J_{CF}$ = 25.3 Hz). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –111.8 (t, $^{3}J_{FF}$ = 5.6 Hz 2F), –111.4 (t, $^{3}J_{FF}$ = 5.6 Hz 2F), –63.1 (s, 3F). HRMS Calcd for $C_{15}H_8F_7Br$ 399.9698, found *m/z* 399.9696.



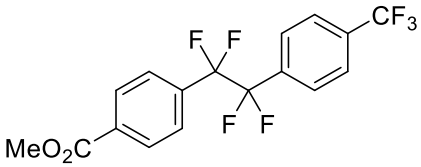
4-(1,1,2,2-Tetrafluoro-2-(4-methoxyphenyl)ethyl)benzotrifluoride (17e): Following the general procedure, the reaction with 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (66.3 mg, 0.30 mmol) was conducted to give the title compound as a white solid (91.8 mg, 87%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 99/1) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 3.85 (s, 3H, –OCH$_3$), 6.93 (d, J = 8.7 Hz, 1H), 7.39 (d, J = 8.7 Hz, 2H), 7.60 (d, J = 8.1 Hz, 2H), 7.69 (d, J = 8.1 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 55.3 (s, –OCH$_3$), 113.8, 116.1 (tt, $^{1}J_{CF}$ = 253.4, $^{2}J_{CF}$ = 37.5 Hz), 116.6 (tt, $^{1}J_{CF}$ = 252.7, $^{2}J_{CF}$ = 35.4 Hz), 123.6 (q, $^{1}J_{CF}$ = 273.4 Hz, –CF$_3$), 125.1 (q, $^{3}J_{CF}$ = 3.7 Hz), 127.6 (t, $^{3}J_{CF}$ = 6.4 Hz), 128.4 (t, $^{3}J_{CF}$ = 6.4 Hz), 133.0 (q, $^{2}J_{CF}$ = 32.7 Hz), 134.7 (t, $^{2}J_{CF}$ = 24.9 Hz), 161.7. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.1 (s, 2F), –110.5 (s, 2F), –63.1 (s, 3F). HRMS Calcd for $C_{16}H_{11}F_7O$ 352.0698, found *m/z* 352.0697.



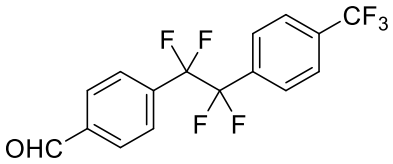
4-(1,1,2,2-Tetrafluoro-2-(4-(N,N-dimethylamino)phenyl)ethyl)benzotrifluoride (17f): Following the general procedure, the reaction with 5,5-dimethyl-2-(4-(N,N-dimethylamino)phenyl)-1,3,2-dioxaborinane (69.9 mg, 0.30 mmol) was conducted to give the title compound as a white solid (98.5 mg, 90%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 99/1) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 3.01 (s, 6H, –N(CH_3)$_2$), 6.67 (d, J = 8.7 Hz, 1H), 7.27 (d, J = 8.7 Hz, 2H), 7.59 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 8.3 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 40.1 (–N(*C*H$_3$)$_2$), 110.9, 116.2 (tt, $^{1}J_{CF}$ = 253.1, $^{2}J_{CF}$ = 38.5 Hz), 116.7 (t, $^{2}J_{CF}$ = 25.7 Hz), 117.1 (tt, $^{1}J_{CF}$ = 252.8, $^{2}J_{CF}$ = 35.3 Hz), 123.6 (q, $^{1}J_{CF}$ = 272.6 Hz, –*C*F$_3$), 125.0 (q, $^{3}J_{CF}$ = 3.6 Hz), 127.6 (t, $^{3}J_{CF}$ = 6.4 Hz), 127.8 (t, $^{3}J_{CF}$ = 6.4 Hz), 132.7 (q, $^{2}J_{CF}$ = 32.5 Hz), 135.1 (t, $^{2}J_{CF}$ = 26.0 Hz), 151.9. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.1 (s, 2F), –110.1 (s, 2F), –62.9 (s, 3F). HRMS Calcd for $C_{17}H_{14}F_7N$ 365.1014, found *m/z* 365.1013.



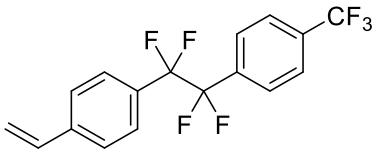
1,1,2,2-Tetrafluoro-1,2-bis(4-(trifluoromethyl)phenyl)ethane (17g): Following the general procedure, the reaction with 2-(4-trifluoromethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (77.4 mg, 0.30mmol) was conducted to give the title compound as a white solid (87.7 mg, 75%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 99/1) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.66 (d, J = 8.3 Hz, 2H), 7.74 (d, J = 8.3 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 115.8 (tt, $^{1}J_{CF}$ = 253.4, $^{2}J_{CF}$ = 37.0 Hz), 122.5 (q, $^{1}J_{CF}$ = 272.5 Hz, –*C*F$_3$), 125.4 (q, $^{3}J_{CF}$ = 3.6 Hz), 127.6 (t, $^{3}J_{CF}$ = 4.1 Hz), 133.4 (q, $^{2}J_{CF}$ = 33.0 Hz), 133.9 (t, $^{2}J_{CF}$ = 25.2 Hz). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –111.5 (s, 4F), –63.1 (s, 6F). HRMS Calcd for $C_{16}H_8F_{10}$ 390.0466, found *m/z* 390.0463.



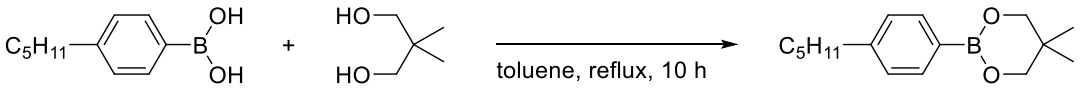
4-(1,1,2,2-Tetrafluoro-2-(4-(methoxycarbonyl)phenyl)ethyl)benzotrifluoride (17h): Following the general procedure, the reaction with 2-(4-(methoxycarbonyl)phenyl)-5,5-dimethyl-1,3,2-dioxaborinane (74.5 mg, 0.30 mmol) was conducted to give the title compound as a white solid (69.5 mg, 61%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 95/5) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 3.95 (s, 3H, $–CO_2CH_3$), 7.57 (d, J = 8.3 Hz, 2H), 7.62 (d, J = 7.9 Hz, 2H), 7.71 (d, J = 7.9 Hz, 2H), 8.11 (d, J = 8.3 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 52.4, 115.9 (tt, $^{1}J_{CF}$ = 253.7, $^{2}J_{CF}$ = 36.1 Hz), 116.0 (tt, $^{1}J_{CF}$ = 253.7, $^{2}J_{CF}$ = 36.9 Hz), 123.4 (q, $^{1}J_{CF}$ = 272.4 Hz, $–CF_3$), 125.3 (q, $^{3}J_{CF}$ = 3.9 Hz), 127.1 (t, $^{3}J_{CF}$ = 6.0 Hz), 127.6 (t, $^{3}J_{CF}$ = 5.9 Hz), 129.4, 132.8, 133.2 (q, $^{2}J_{CF}$ = 32.8 Hz), 134.1 (t, $^{2}J_{CF}$ = 25.4 Hz), 134,4 (t, $^{2}J_{CF}$ = 24.5 Hz), 166.0. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –111.8 (s, 2F), –111.8 (s, 2F), –63.1 (s, 3F). HRMS Calcd for $C_{17}H_{11}F_7O_2$ 380.0647, found *m/z* 380.0650.



4-(1,1,2,2-Tetrafluoro-2-(4-formylphenyl)ethyl)benzotrifluoride (17i): Following the general procedure, the reaction with 2-(4-formylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (65.4 mg, 0.30 mmol) was conducted to give the title compound as a white solid (86.0 mg, 82%). Purification was conducted by flash column chromatography with hexane/ethyl acetate (v/v' = 95/5) as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 7.65 (d, J = 8.2 Hz, 2H), 7.70 (d, J = 8.5 Hz, 2H), 7.73 (d, J = 8.5 Hz, 2H), 7.97 (d, J = 8.2 Hz, 2H), 10.10 (s, 1H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 115.9 (tt, $^{1}J_{CF}$ = 253.8, $^{2}J_{CF}$ = 37.1 Hz), 115.9 (tt, $^{1}J_{CF}$ = 253.8, $^{2}J_{CF}$ = 37.1 Hz), 123.5 (q, $^{1}J_{CF}$ = 272.7 Hz, $–CF_3$), 125.3 (q, $^{3}J_{CF}$ = 3.7 Hz), 127.6 (t, $^{3}J_{CF}$ = 6.1 Hz), 127.8 (t, $^{3}J_{CF}$ = 6.1 Hz), 129.3, 133.4 (q, $^{2}J_{CF}$ = 32.6 Hz), 133.9 (t, $^{2}J_{CF}$ = 24.8 Hz), 135.8 (t, $^{2}J_{CF}$ = 24.5 Hz), 138.2, 191.3. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –111.6 (t, J_{FF} = 6.3 Hz, 2F), –111.5 (t, J_{FF} = 6.3 Hz, 2F), –63.1 (s, 3F). HRMS Calcd for $C_{16}H_9F_7O$ 350.0542, found *m/z* 350.0541.

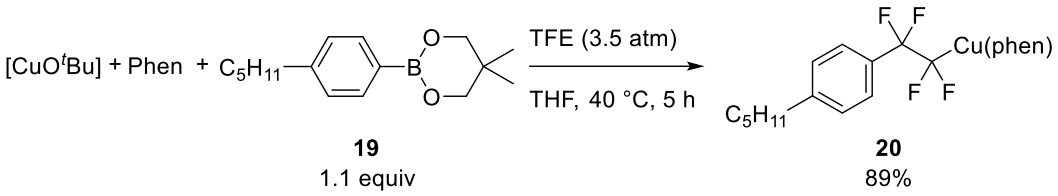


4-(1,1,2,2-Tetrafluoro-2-(4-vinylphenyl)ethyl)benzotrifluoride (17j): Following the general procedure, the reaction using 5,5-dimethyl-2-(4-vinylphenyl)-1,3,2-dioxaborinane (64.8 mg, 0.30 mmol) was conducted to give the title compound as a white solid (98.3 mg, 94%). Purification was conducted by flash column chromatography with 99:1 hexane : ethyl acetate as the eluent. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 5.38 (d, J = 10.9 Hz, 1H), 5.85 (d, J = 17.4 Hz, 1H), 6.75 (dd, J = 17.4, 10.9 Hz, 1H), 7.44 (d, J = 8.6 Hz, 2H), 7.47 (d, J = 8.6 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H), 7.71 (d, J = 8.3 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 116.0 (tt, $^{1}J_{CF}$ = 253.5, $^{2}J_{CF}$ = 37.0 Hz), 116.2, 116.4 (tt, $^{1}J_{CF}$ = 252.9, $^{2}J_{CF}$ = 35.9 Hz), 123.6 (q, $^{1}J_{CF}$ = 272.2 Hz, –CF$_3$), 125.2 (q, $^{3}J_{CF}$ = 3.7 Hz), 126.0, 127.1 (t, $^{3}J_{CF}$ = 6.4 Hz), 127.6 (t, $^{3}J_{CF}$ = 6.3 Hz), 129.3 (t, $^{2}J_{CF}$ = 24.9 Hz), 133.1 (q, $^{2}J_{CF}$ = 32.8 Hz), 134.5 (t, $^{2}J_{CF}$ = 24.9 Hz), 135.7, 140.4. ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –111.9 (s, 2F), –111.3 (s, 2F), –63.0 (s, 3F). HRMS Calcd for $C_{17}H_{11}F_7$ 348.0749, found *m/z* 348.0750.



18 1.1 equiv **19** 95%

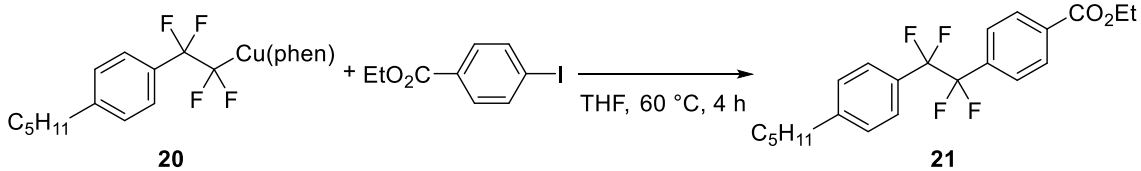
Preparation of 5,5-dimethyl-2-(4-pentylphenyl)-1,3,2-dioxaborinane (19): To a solution of 2,2-dimethyl-1,3-propandiol (3.25 g, 31.2 mmol) in 100 mL of toluene, 4-(pentyl)phenylboronic acid (**18**: 5.00 g, 26.0 mmol) was added. The mixture was heated under reflux for 10 h. After the addition of water, the product was extracted with $CHCl_3$ three times. The combined organic layer was washed with brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent under reduced pressure afforded 5,5-dimethyl-2-(4-pentylphenyl)-1,3,2-dioxaborinane (**19**: 6.43 g, 24.7 mmol, 95%) as an analytically pure white solid. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 0.89 (t, J = 6.5 Hz, 3H), 1.03 (s, 6H), 1.33 (m, 4H), 1.63 (m. 2H), 2.62 (t, J = 7.4 Hz, 2H), 3.77 (s, 4H), 7.19 (d, J = 7.7 Hz, 2H), 7.73 (d, J = 7.7 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 14.0, 21.9, 22.5, 31.0, 31.5, 31.8, 36.0, 72.2, 127.7, 133.8, 145.7. ^{11}B NMR (128 MHz, in $CDCl_3$, rt, δ/ppm): 26.7 (br). HRMS Calcd for $C_{16}H_{25}O_2B$ 260.1948, found *m/z* 260.1950.



19
1.1 equiv

20
89%

Carbocupration of 19 with TFE: To a solution of [CuO^{t}Bu] (267 mg, 2.00 mmol) and Phen (360 mg, 2.00 mmol) in 20 mL of THF, **19** (572 mg, 2.20 mmol) was added. The resultant solution was transferred into an autoclave reactor, and then TFE (3.5 atm) was charged into the reactor. After the reaction mixture was heated at 40 °C for 5 h, all volatiles were removed under reduced pressure. The resultant solid was washed with diethyl ether three times to give (phen)CuCF_2CF_2(4-(C_5H_{11})C_6H_4) as an orange solid (**20**: 871 mg, 1.78 mmol, 89%). NMR spectra of **20** reflects the equilibrium between a neutral [(phen)CuCF_2CF_2(4-C_5H_{11})C_6H_4] (**20-n**) and an ionic form [(phen)$_2$Cu][Cu(CF_2CF_2(4-C_5H_{11})C_6H_4)$_2$] (**20-i**). For **20-n**, ^{1}H NMR (400 MHz, THF-d_8, rt, δ/ppm): 0.89 (t, J = 6.6 Hz, 3H), 1.34 (m, 4H), 1.63 (m. 2H), 2.61 (t, J = 7.4 Hz, 2H), 7.14 (d, J = 8.3 Hz, 2H, Ar), 7.54 (d, J = 8.3 Hz, 2H, Ar), 7.89 (m, 2H), 8.01 (br, 2H), 8.57 (br, 2H), 9.03 (br, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in THF-d_8, rt, δ/ppm): 14.3, 23.4, 32.1, 32.5, 36.5, 126.1, 127.6, 127.9 (Ar), 128.0 (t, $^3J_{CF}$ = 5.6 Hz, Ar), 129.9, 135.4 (t, $^2J_{CF}$ = 27.8 Hz, Ar), 138.5, 143.9 (Ar), 144.9, 151.1. The peaks assigned to CF_2CF_2 moiety were not clearly observed due to their multiple coupling. ^{19}F NMR (376 MHz, THF-d_8, rt, δ/ppm): –111.5 (br, 2F), –108.1 (br, 2F). The peaks assigned to a minor isomer **20-i** were not distinctly observed due to their weak intensity and the overlap with other peaks.

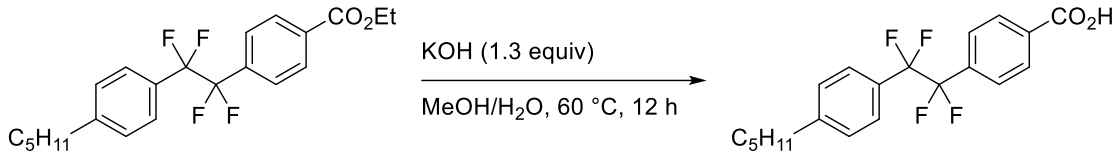


20
1.2 equiv

21
94%

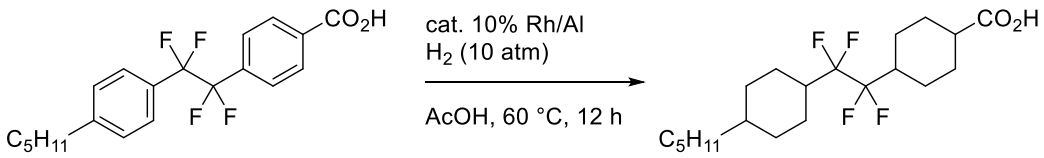
Coupling reaction of 20 with 4-ethoxycarbonyl-1-iodobenzene: To a suspension of **20** (871 mg, 1.77 mmol) in 20 mL of THF, 4-ethoxycarbonyl-1-iodobenzene (414 mg, 1.50 mmol) was added. The mixture was heated at 60 °C for 4 h. 30 mL of hexane was added, and then the resultant mixture stirred at room temperature for 10 min. The mixture was filtrated, and concentrated under reduced pressure to give ethyl 4-(1,1,2,2-tetrafluoro-2-(4-pentylphenyl)ethyl)benzoate (**21**: 575 mg, 1.45 mmol, 94%)

as an analytically pure white solid. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 0.90 (t, *J* = 6.9 Hz, 3H), 1.23-1.37 (m, 4H), 1.41 (q, *J* = 7.2 Hz, 3H, –OCH_2CH_3), 1.62 (tt, *J* = 7.3 Hz, 7.5 Hz, 2H), 2.64 (t, *J* = 7.7 Hz, 2H), 4.41 (q, *J* = 7.2 Hz, 2H, –OCH_2CH_3), 7.22 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.3 Hz, 2H), 8.07 (d, *J* = 8.3 Hz, 2H). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.2 (s, 2F), –111.3 (s, 2F). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 13.9, 14.2, 22.4, 30.8, 31.4, 35.7, 61.3, 116.3 (tt, $^{1}J_{CF}$ = 254.3, $^{2}J_{CF}$ = 36.7 Hz), 116.6 (tt, $^{1}J_{CF}$ = 253.6, $^{2}J_{CF}$ = 35.4 Hz), 126.8 (t, $^{3}J_{CF}$ = 6.1 Hz), 127.1 (t, $^{3}J_{CF}$ = 6.3 Hz), 127.6 (t, $^{2}J_{CF}$ = 25.1 Hz), 128.1, 129.1, 132.8, 135.2 (t, $^{2}J_{CF}$ = 25.0 Hz), 146.3, 165.7. HRMS Calcd for $C_{22}H_{24}F_4O_2$ 396.1712 found *m/z* 396.1711.



21 **22**
97%

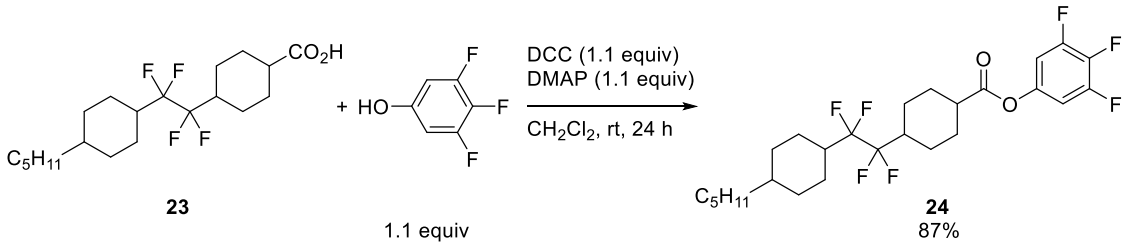
Hydrolysis of 21: To a suspension of **21** (472 mg, 1.19 mmol) in 5.0 mL of MeOH/H_2O (v/v' = 1/1), potassium hydroxide (84.2 mg, 1.50 mmol) was added. The mixture was heated at 60 °C for 12 h. After the addition of 1 M HCl, the product was extracted with $CHCl_3$ three times. The combined organic layer was washed with brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent under reduced pressure afforded 4-(1,1,2,2-tetrafluoro-2-(4-pentylphenyl)ethyl)benzoic acid (**22**: 426 mg, 1.16 mmol, 97%) as an analytically pure white solid. ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 0.90 (t, *J* = 6.8 Hz, 3H), 1.29-1.36 (4H), 1.63 (m, 2H), 2.64 (t, *J* = 7.7 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 8.15 (d, *J* = 8.3 Hz, 2H). ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –112.3 (s, 2F), –111.2 (s, 2F).



22 **23**
95%

Hydrogenation of 22: A suspension of **22** (201 mg, 0.546 mmol) in AcOH (5.0 mL) was hydrogenated under H_2 (10 atm) with a catalytic amount of 10% Rh/Al (25 mg) at 60 °C for 12 h. After the filtration of the catalyst, the removal of the solvent gave 4-(1,1,2,2-tetrafluoro-2-(4-pentylcyclohexyl)ethyl)cyclohexyane-1-carboxylic acid (**23**:

198 mg, 0.520 mmol, 95%) as a white solid. The product was obtained as a mixture of geometrical isomers, which made it difficult to identify **23** by NMR analysis. The product was used in the next reaction without further purification.



Esterification of 23 with 3,4,5-trifluorophenol: To a solution of **23** (198 mg, 0.520 mmol), 3,4,5-trifluorophenol (84.7 mg, 0.572 mmol), and DMAP (69.9 mg, 0.572 mmol) in 20 mL of CH_2Cl_2, DCC (118.0 mg, 0.572 mmol) was added. The resultant solution was stirred at room temperature for 24 h. The crude product was purified by column chromatography with hexane/EtOAc (v/v' = 95/5) as the eluent to afford 3,4,5-trifluorophenyl 4-(1,1,2-2-tetrafluoro-2-(4-pentylcyclohexyl)ethyl)cyclohexane-1-carboxylate (**24**, 242 mg, 87%) as a mixture of geometrical isomers. The major isomer was isolated by HPLC as a white solid (104 mg, 0.204 mmol, 39%). ^{1}H NMR (400 MHz, in $CDCl_3$, rt, δ/ppm): 0.89 (t, J = 6.8 Hz, 3H), 1.21-1.38 (8H), 1.42-1.74 (13H), 1.92 (d, J = 12.4 Hz, 2H), 2.12 (m, 2H), 2.31 (d, J = 12.4 Hz, 2H), 2.89 (m, 1H), 6.79 (dd, J_{HF} = 7.6, 6.1 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 MHz, in $CDCl_3$, rt, δ/ppm): 14.0, 20.0, 21.5, 22.7, 26.2, 27.3, 29.0, 31.4, 32.0, 32.6, 38.9, 39.6 (t, $^{2}J_{CF}$ = 22.3 Hz), 39.9 (t, $^{2}J_{CF}$ = 21.6 Hz), 106.9 (m), 119.9 (tt, $^{1}J_{CF}$ = 252.7, $^{2}J_{CF}$ = 36.7 Hz), 120.5 (tt, $^{1}J_{CF}$ = 252.1, $^{2}J_{CF}$ = 35.4 Hz), 138.0 (dt, $^{1}J_{CF}$ = 249.7, $^{2}J_{CF}$ = 15.2 Hz), 145.4 (td, $^{3}J_{CF}$ = 11.7, $^{4}J_{CF}$ = 4.4 Hz), 151.0 (ddd, $^{1}J_{CF}$ = 251.1, $^{2}J_{CF}$ = 10.9, $^{3}J_{CF}$ = 5.2 Hz), ^{19}F NMR (376 MHz, in $CDCl_3$, rt, δ/ppm): –163.7 (tt, $^{3}J_{FF}$ = 20.7 Hz, $^{4}J_{HF}$ = 6.1 Hz, 1F), –132.9 (dd, $^{3}J_{FF}$ = 20.7 Hz, $^{3}J_{HF}$ = 7.6 Hz, 2F), –115.8 (br, 2F), –115.1 (br, 2F). HRMS (CI) Calcd for $C_{26}H_{33}F_7O_2$ [M+H] 511.2442, found *m/z* 511.2445.

4.9 References and notes

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Conclusion

Described in this thesis were the studies on the transformation reaction of tetrafluoroethylene with palladium or copper complexes. The studies enable efficient and straightforward transformations of tetrafluoroethylene into more valuable organofluorine compounds. Fluorinated palladium or copper complexes generated by the reaction of tetrafluoroethylene with palladium or copper complex are found to play crucial roles in the transformation reactions.

In chapters 2 and 3, Pd(0)-catalyzed base-free Suzuki-Miyaura or Hiyama coupling reactions of tetrafluoroethylene were described. A variety of trifluorostyrene derivatives were prepared directly from tetrafluoroethylene. Mechanistic study indicated that the base-free coupling reactions would proceed through a trifluorovinyl fluoropalladium complex generated by the oxidative addition of a C−F bond of tetrafluoroethylene. The complex are reactive enough toward neutral organoboron compounds or organosilicon reagents, which enables the coupling reactions to proceed without base. It was found that the base-free system through reactive transition-metal fluoride intermediate is applicable to other fluoroalkenes and fluoroarenes.

In chapter 4, the method to construct a tetrafluoroethylene-bridging structure with copper complex was described. A key synthetic intermediate in the transformation is a fluoroalkylcopper(I) complex generated by carbocupration of tetrafluoroethylene. The complex was isolated and characterized by means of X-ray diffraction analysis and NMR analysis. With the complex as a fluoroalkylation reagent, a variety of compounds bearing tetrafluoroethylene-bridging structure were synthesized in high yield. The synthetic utility of the method was demonstrated by straightforward synthesis of a liquid-crystalline compounds bearing a tetrafluoroethylene-bridging structure.

The studies in the thesis will provide new strategies of the transformation of tetrafluoroethylene in organic synthesis and in organofluorine industry. The studies also provide important insight into the transformation reactions of organofluorine compounds with transition-metal complexes.

List of Publications

1. Palladium-Catalyzed Base-Free Suzuki-Miyaura Coupling Reactions of Fluorinated Alkenes and Arenes via a Palladium Fluoride Key Intermediate
   Masato Ohashi, Hiroki Saijo, Mitsutoshi Shibata, Sensuke Ogoshi
   Eur. J. Org. Chem. **2013**, 443–447.
2. 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.
3. Fluoroalkylcopper(I) Complexes Generated by the Carbocupration of Tetrafluoroethylene: Construction of a Tetrafluoroethylene-Bridging Structure
   Hiroki Saijo, Masato Ohashi, Sensuke Ogoshi
   J. Am. Chem. Soc. **2014**, *136*, 15158–15161.

Supplementary Publications

1. Nickel(0)-Catalyzed Formation of Oxaaluminacyclopentenes via an Oxanickelacyclopentene Key Intermediate: Me_2AlOTf-Assisted Oxidative Cyclization of an Aldehyde and an Alkyne with Nickel(0)
   Masato Ohashi, Hiroki Saijo, Tomoya Arai, Sensuke Ogoshi
   Organometallics **2010**, *29*, 6534–6540.
2. Palladium-catalyzed coupling reactions of tetrafluoroethylene with arylzinc compounds
   Masato Ohashi, Tadashi Kambara, Tsubasa Hatanaka, Hiroki Saijo, Ryohei Doi, Sensuke Ogoshi
   J. Am. Chem. Soc. **2011**, *133*, 3256–3259.
3. Carbon-Fluorine Bond Activation of Tetrafluoroethylene on Palladium(0) and Nickel(0): Heat or Lewis Acidic Additive Promoted Oxidative Addition
   Masato Ohashi, Mitsutoshi Shibata, Hiroki Saijo, Tadashi Kambara, Sensuke Ogoshi
   Organometallics **2013**, *32*, 3631–3639.