Doctoral Dissertation

Studies on Synthesis of Fluoroalkyl Compounds via Addition of Metal Species to Tetrafluoroethylene

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Contents

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 2015 to March 2021. The thesis describes Ni(0)-catalyzed multi-component transformations with tetrafluoroethylene via the oxidative cyclization as a key reaction step.

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List of Abbreviations

Ac	acetyl
anal.	elemental analysis
Ar	aryl
atm	atmospheric pressure
br	broad
Bu	butyl
calcd	calculated
cat.	catalyst
CI	chemical ionization
°C	degrees Celsius
d	doublet
d	deuterated
DMA	*N*,*N*-dimethylacetamide
DMF	*N*,*N*-dimethylformamide
DMI	1,3-Dimethyl-2-Imidazolidinone
δ	chemical shift of NMR signal in ppm
e.g.	for example
eq.	equivalent
EI	electron ionization
Et	ethyl
ETFE	ethylene-tetrafluoroethylene copolymer
GC	gas chromatography
GWP_{100}	global warming potential
h	hour(s)
HPLC	high performance liquid chromatography
HRMS	high-resolution mass spectrometry
Hz	hertz
i	iso
IPr	1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene
IPrCl	1,3-bis(2,6-diisopropylphenyl)-4,5-dichloro-imidazol-2-ylidene
J	coupling constant in NMR
L	ligand
m	multiplet
m	meta

min.	minute(s)
mL	milliliter
M	metal
Me	methyl
Mes	Mesityl
n	normal
neop	neopentyl
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
o	ortho
ORTEP	Oak Ridge thermal ellipsoid plot
p	para
Ph	phenyl
Phen	1,10-phenanthroline
pin	pinacolato
Pr	propyl
PTFE	poly-tetrafluoroethylene
q	quartet
quant.	quantitative
rt	room temperature
s	singlet
t	triplet
t	tertiary
temp.	temperature
TFE	tetrafluoroethylene
THF	tetrahydrofuran
TMS	trimethylsilyl

Chapter 1

General Introduction

1.1. Introduction

Organic molecules that contain fluorine atom(s) have attracted much attention in various areas such as pharmaceuticals and agrochemicals owing to their unique properties and bioactivities that originate from the electronegativity and atomic size of fluorine (Figure 1.1).[1] Therefore, a great deal of research has been devoted to the development of synthetic methods that enable to introduce fluorine atom(s), especially trifluoromethyl group, into organic compounds.[2] On the other hand, the method for the introduction of longer-chain fluoroalkyl groups was largely unexplored due to i) the usually high cost of reagents and ii) the limited availability of suitable substrates.

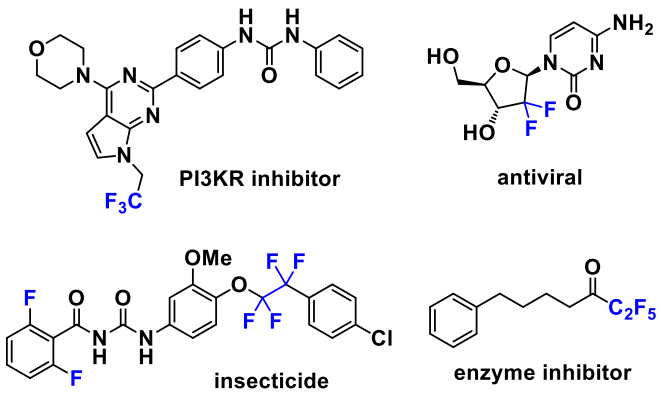


Figure 1.1. Fluoroalkyl group-containing biologically active compounds

On the other hand, the transformation of industrially available perfluorinated compounds into a variety of highly fluorinated organic compounds is a more straightforward approach.[3]

1.2 Tetrafluoroethylene (TFE)

For the synthesis of such polyfluorinated compounds, tetrafluoroethylene (TFE) is one of the ideal starting materials as it is an economical feedstock in the fluorine industry and environmentally benign with a negligible GWP_{100} (Figure 1.2).[4] However, the use of

TFE has been limited mostly to the production of polytetrafluoroethylene (PTFE) and copolymers with other alkenes such as ethylene-TFE copolymer (ETFE).[5] Considering the limitation, methods for the efficient transformation of TFE have been explored extensively.

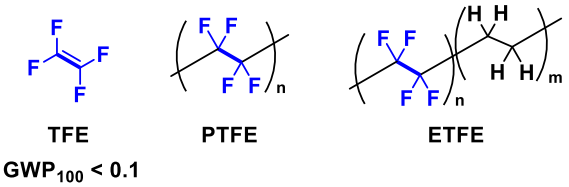
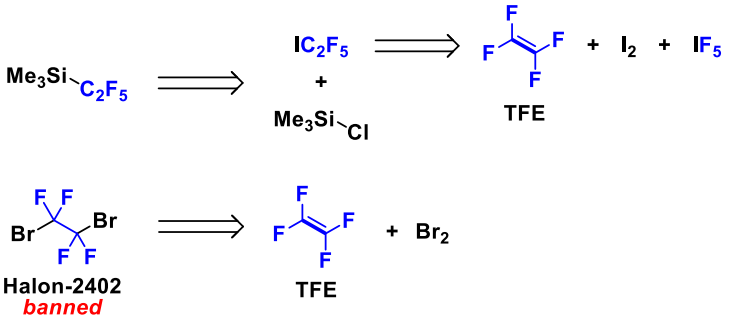


Figure 1.2. TFE containing fluoropolymers

1.3 TFE as a starting material.

Although the number of examples is small, TFE has been used for the synthesis of fluoroalkylation reagents (Scheme 1.1). For instance, a pentafluoroethylation reagent TMS–C_2F_5 and its precursor IC_2F_5 were synthesized from TFE.[6] In addition, Halon-2402 (1,2-dibromo-1,1,2,2-tetrafluoroethane), which was employed for the synthesis of tetrafluoroethylene-bridged compounds has also been synthesized from TFE.[7] However, Halon-2402 is already banned in countries that have ratified the Montreal Protocol on account of its global warming potential (GWP_{100}; 1470) and ozone depletion potential (ODP; 6) values,[8] Therefore, he direct use of TFE for fluoroalkylation reactions can potentially reduce the reaction steps required and the quantity of chemical waste produced.

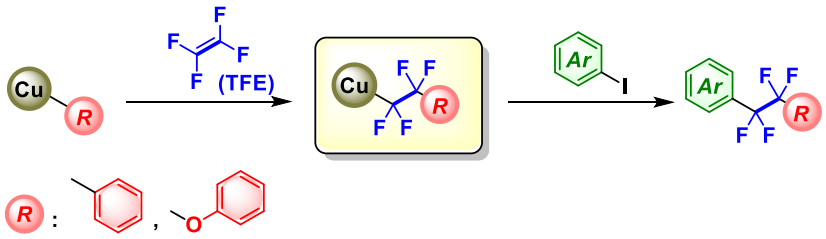


Scheme 1.1. TFE as starting materials for fluoroalkylation reagents

1.4 Addition of copper(I)-species to TFE

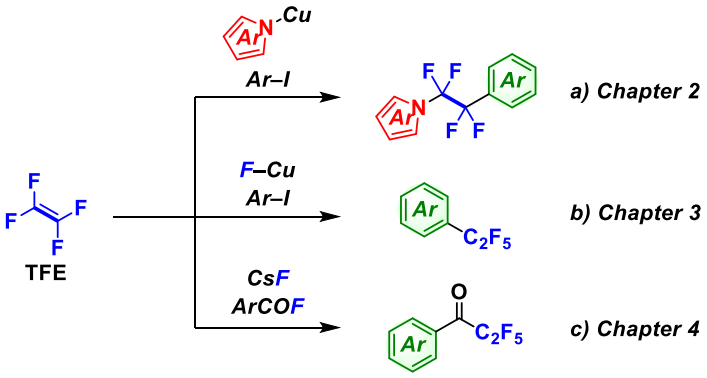
Our group has been developing a series of transformations of TFE into valuable organofluorine compounds. Among them, we have already demonstrated that TFE can serve as an ideal C2 building block for the introduction of fluorinated functional groups,

such as $–CF_2CF_2–$,[9] and $–CF=CF_2$[9,10] into organic molecules using copper(I) complexes. In these copper(I)-mediated transformations of TFE into 1,2-diaryl-tetrafluoro-ethane derivatives, the carbocupration of TFE is a key elementary step.[9a] In addition, we have demonstrated that the carbocupration can be successfully expanded to the related oxycupration of TFE, which led to a variety of fluoroalkyl ethers (Scheme 1.2).[9b] The addition to TFE was also observed when silyl- or borylcopper was employed.[10b,c] In this context, I speculated that other metal species could add to TFE to give the corresponding fluorometal species which is useful for the introduction of fluoroalkyl group into organic compounds.



Scheme 1.2. Copper(I)-mediated synthesis of tetrafluoroethylene-bridged compounds

In this thesis, the purpose of this study is to develop the methodology for the synthesis of fluoroalkyl compounds via addition of metal species to TFE. This thesis consists of the general introduction and the following three chapters (Scheme 1.3). In Chapter 2, one-pot synthesis of *N*-tetrafluoroethylated heteroarenes via azacupration of TFE is described (Scheme 1.3a). Chapter 3 deals with a copper-catalyzed pentafluoroethylation of iodoarenes via fluorocupration of TFE (Scheme 1.3b). In chapter 4, the development of a CsF-catalyzed Fluoroacylation of TFE is discussed (Scheme 1.3c). Finally, this thesis is summarized in conclusion.



Scheme 1.3. This thesis describes a) one-pot synthesis of *N*-fluoroalkyl heteroarenes via azacupration/coupling pathway b) Cu(I)-catalyzed pentafluoroethylation of iodoarenes via fluorocupration of TFE c) CsF-catalyzed catalytic pentafluoroethylation of acyl fluorides

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Chapter 2

One-Pot Synthesis of *N*-Tetrafluoroethylated Heteroarenes from Tetrafluoroethylene via Azacupration/Coupling Pathway

2.1 Introduction

N-fluoroalkylation of nitrogen-atom-containing organic compounds has been recognized as a powerful method for the development of high-performance bioactive compounds such as pharmaceuticals, as fluoroalkyl groups can enhance lipophilicity and metabolic stability.[1] Therefore, significant effort has been devoted to the development of efficient synthetic methods for *N*-fluoroalkylation. However, almost all these have focused on the functionalization using trifluoromethyl (CF_3) groups or CF_3-terminated fluoroalkyl moieties (Figure 2.1).[2]

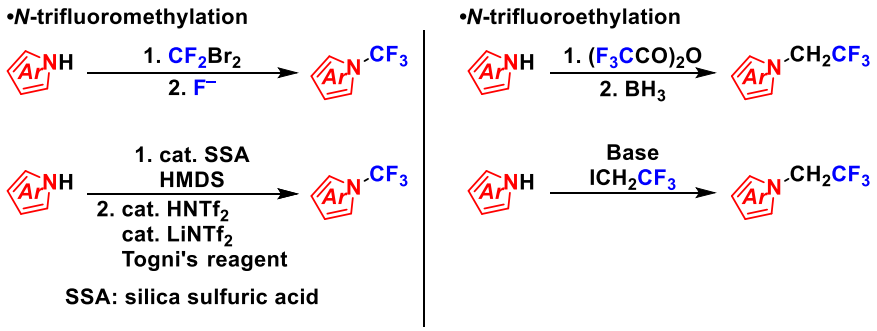
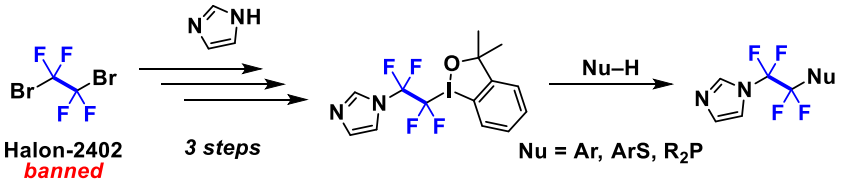


Figure 2.1. Fluoroalkylation of *N*-heteroarenes

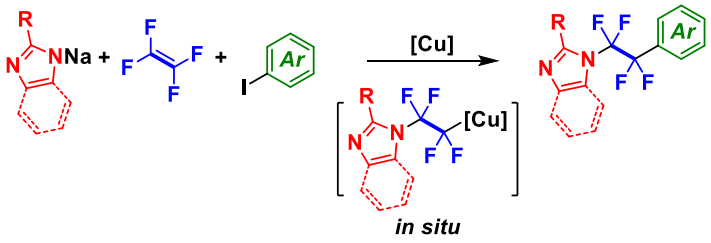
The construction of molecular structures bridged by fluoroalkyl motifs such as tetrafluoroethylene (–CF_2CF_2–) remains uncommon because the synthetic routes to such compounds are limited, and multi-step reactions are often required (Scheme 2.1).[3] 1,2-Dibromotetrafluoroethane (Halon-2402) has been widely employed for the synthesis of tetrafluoroethylene skeletons. However, the production of Halon-2402 is now banned in countries that have ratified the Montreal Protocol on account of its global warming potential (GWP100; 1470) and ozone depletion potential (ODP; 6) values.[4] Thus, it is important to develop an alternative synthetic strategy to replace the previous methods.



Scheme 2.1. Synthesis of *N*-tetrafluoroethylene compounds

TFE is used as a chemical feedstock for the production of fluoropolymers in the chemical industry. The GWP_{100} and ODP values of TFE are negligible compared to those of Halon-2402.[5] Therefore, TFE is an ideal starting material for the production of 1,2-difunctionalized tetrafluoroethane derivatives. As mentioned in General Introduction, our group has demonstrated 1,2-diflunctionalization of TFE using the corresponding electrophile and copper(I)-species.[6] In this literature, it was disclosed a new difunctionalization reaction of TFE using the azacupration of copper(I) imidazolide species followed by coupling with an aryl iodide.

Described in this Chapter is one-pot copper(I)-mediated synthesis of 2-aryl-(1-*N*-heteroaryl)-1,1,2,2-tetrafluoroethane derivatives through azacupration and coupling reaction process (Scheme 2.2). The present system could be a new route to *N*-tetrafluoroethylene compounds without the use of Halon-2402.

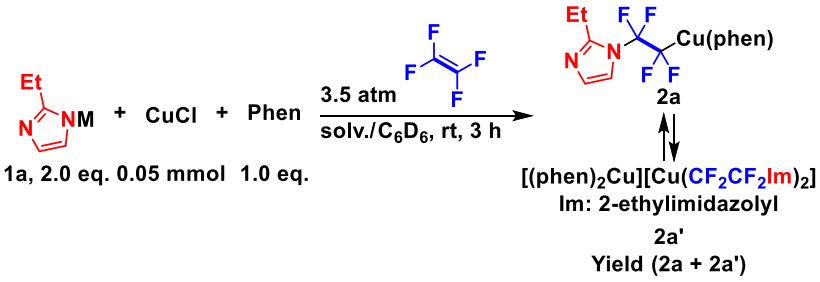


Scheme 2.2. One-pot synthesis of *N*-tetrafluoroethylene-bridged compounds

2.2 Optimization of reaction condition

The reaction using stoichiometric amounts of Phen and CuCl as well as two equivalents of potassium 2-ethylimidazolide (**1a•K**) in DMF/C_6D_6 (4/1, v/v) at room temperature for 3 h gave an equilibrium mixture of the neutral complex [(phen)CuCF_2CF_2Im] (Im: 2-ethylimidazolyl) (**2a**) and the ionic complex [$(phen)_2$Cu][Cu$(CF_2CF_2Im)_2$] (**2a′**) as observed by ^{19}F NMR spectroscopy (Table 2.1 entry 1). The combined yield of these complexes was high (**2a**/**2a′** = 75:25; 88%).[6a,c,e,7] A comparison of this ratio of **2a** and **2a′ (2a**/**2a′** = 86:14; 83% yield), which was observed after 30 min, indicates that the neutral complex **2a** was produced first, followed by the generation of the ionic complex **2a′**. This behavior is consistent with that of a reported trifluoromethyl copper complex.[7a] Next, several solvents were tested for this reaction system (entries 2–4). The use of aprotic polar solvents such as DMA and DMI resulted in slightly lower yields than when using DMF (entry 2: DMA, 67%; entry 3: DMI, 83%), while using THF provided **2a** and **2a′** in low yield (entry 4: 6%). Moreover, a trifluorovinyl species, which would be a trifluorovinyl imidazole derivative, was detected as a side product in the ^{19}F NMR spectrum (12%). This result suggests that β-fluorine elimination occurred from the imidazole-substituted tetrafluoroethylene copper(I) complexes **2a** or **2a′**.[6c,8] The aprotic polar solvent DMF is thus important to prevent this β-fluorine elimination by coordinating to Na cation and decreasing its Lewis acidity. The reaction using the sodium imidazolide **1a•Na** instead of the potassium salt **1a•K** gave the desired complexes **2a** and **2a′** in quantitative yield (entry 5: 99%). The total yield of **2a** and **2a′** was reduced when the reaction was performed in the absence of Phen (entry 6, 87%).[6c]

Table 2.1. Optimization of reaction conditions

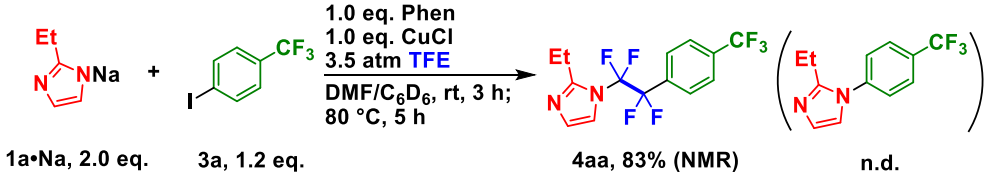


entry	M	Solvent	Yield / %[a,b]
1	K (1a•K)	DMF	88
2	K (1a•K)	DMA	67
3	K (1a•K)	DMI	83
4	K (1a•K)	THF	6
5	Na (1a•K)	DMF	99
6[c,d]	Na (1a•K)	DMF	87

[a]Total yield of 2a and 2a'. [b]Yields were determined based on the ^{19}F NMR spectra using $PhCF_3$ as an internal standard. [c]Without Phen. [d]Total yield of $CuCF_2CF_2Im$ and $[(DMF)_nNa][Cu(CF_2CF_2Im)_2]$.[ref7]

2.3 One-pot synthesis of *N*-tetrafluoroethylene compound

Considering C_{Ar}–N bond formation using copper complex requires high reaction temperature,[9] we envisioned that one-pot synthesis of 2-aryl-1-(*N*-heteroaryl)-1,1,2,2-tetrafluoroethane could proceed by adding an iodoarene into the reaction mixture in Table 2.1. The reaction mixture of Phen, CuCl, sodium 2-ethylimidazolide (**1a•Na**), and 4-trifluoromethyl iodobenzene (**3a**) in DMF/C_6D_6 (4/1, v/v) solution was exposed to TFE (3.5 atm) at room temperature for 3 h and then heated at 80 °C for 5 h. The corresponding *N*-tetrafluoroethylated product (**4aa**) was generated in high yield (83%) (Scheme 2.3). In this reaction, no product derived from C‑N coupling between imidazolide **1a** and iodoarene **3a** was observed. This result indicates that this reaction can be applied for the one-pot synthesis of *N*-fluoroalkyl heteroarenes.

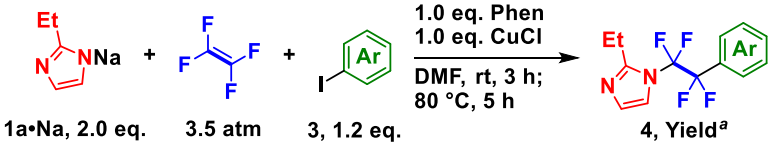


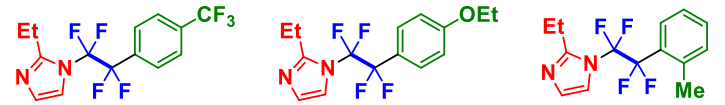
Scheme 2.3. One-pot synthesis of **4aa**

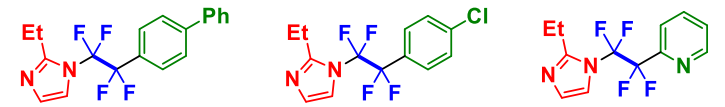
2.4 Substrate scope (iodoarenes)

With the one-pot reaction conditions in hand, the three-component coupling reaction was carried out using various aryl iodides (Table 2.2.). Reactions using aryl iodides bearing an electron-withdrawing group at the para position (**3a**) gave the corresponding *N*-fluoroalkyl arene in high yield (**4aa**: 72%). In contrast, aryl iodide **3b** with an electron-donating ethoxy group at the para position furnished **4ab** in low yield (38%). In our previous fluoroalkylation of iodoarenes, iodoarenes bearing electron-donating group(s) show lower reactivities than those with electron-withdrawing group(s) in the coupling reaction with fluoroalkyl copper complexes.[6a,c] The sterically hindered aryl iodide **3c** also showed low reactivity to provide **4ac** in merely 26% yield. When 4-iodobiphenyl (**3d**) was employed, the yield of **4ad** was moderate (56%). The reaction of aryl iodide **3e**, which bears a chloride moiety, occurred selectively at the iodine moiety to afford **4ae** in good yield (**4ae**: 62%). Furthermore, product **4af**, in which two different heteroaromatic moieties are bridged by a tetrafluoroethylene skeleton, was obtained in excellent yield (98%).

Table 2.2 Substrate Scope of iodoarenes





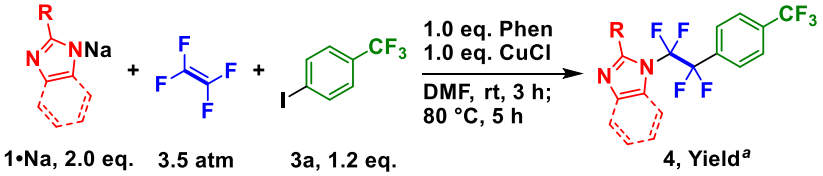


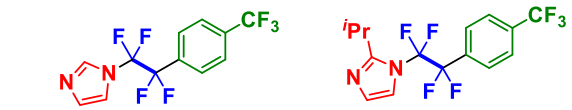
[a] Isolated yield.

2.5 Substrate scope (imidazolides)

The scope of sodium imidazolide/benzimidazolide compounds **1•Na** with aryl iodide **3a** was investigated (Table 2.3). When sodium imidazolide (**1b•Na**) was employed, **4ba** was furnished in good yield (**4ba**, 63%). A sodium imidazolide with an isopropyl moiety (**1c•Na**) also gave the corresponding tetrafluoroethylene-bridged product in good yield (**4ca**, 68%). The reaction of a sodium imidazolide bearing an undecyl group (**1d•Na**) also furnished the corresponding coupling product in moderate isolated yield (**4da**, 51%). The reaction using sodium benzimidazolide (**1e•Na**) instead of an imidazolide gave the corresponding tetrafluoroethylene-bridged product (**4ea**) in good yield (**4ea**, 61%).

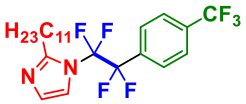
Table 2.3. Substrate scope of sodium imidazolide derivatives



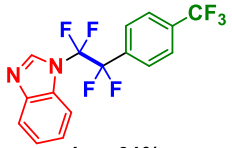


4ba, 63%

4ca, 68%



4da, 51%



4ea, 61%

[a]Isolated yield.

2.6 Conclusion

In Chapter 2, a new copper(I)-mediated one-pot C–N/C–C bond-forming reaction for TFE with various imidazolide salts and aryl iodides is described. The azacupration of TFE using *in-situ*-generated copper(I) imidazolide species to form a fluoroalkyl copper(I) species is a key step for this reaction. this process does not require Halon-2402, which is prohibited by the Montreal Protocol and multi-step reaction to synthesize *N*-tetrafluoroethylene skeleton.

2.7 References and notes

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2.8 Experimental section

General remarks compatible to all the experimental part in this thesis

All manipulations were conducted under a nitrogen atmosphere using dry box techniques otherwise mentioned. ^{1}H, ^{13}C, and ^{19}F nuclear magnetic resonance spectra were recorded on Bruker Avance III 400 and 600 spectrometer. The chemical shifts were recorded relative to residual solvent peaks ($CDCl_3$: δ 7.26 for ^{1}H and δ 77.0 for ^{13}C, CD_3CN: δ 1.94 for ^{1}H and δ 1.3 for ^{13}C, DMF-d_7: δ 2.92 for ^{1}H and δ 29.8 for ^{13}C, DMSO-d_6: δ 2.50 for ^{1}H and δ 39.5 for ^{13}C) or to external standards (α,α,α-trifluorotoluene ($PhCF_3$): δ –65.4 for ^{19}F). High resolution mass spectrometry (HRMS) was performed at Instrumental Analysis Center, Faculty of Engineering, Osaka University. Gel permeation chromatography (GPC) was performed on Japan Analytical Industry LC9225NEXT HPLC system equipped with JAIGEL1H and JAIGEL-2H. Medium-pressure column chromatography was carried out on a Biotage Flash Purification System Isolera, equipped with a 250 nm UV detector. Gas Chromatography - Mass spectrometry (GC-MS) was performed on SHIMADZU GCMS-QP2010 SE. Elemental analyses were performed at Instrumental Analysis Center, Faculty of Engineering, Osaka University. X-ray diffraction data were collected on a two-dimensional X-ray detector (PILATUS 200K/R) equipped in Rigaku XtaLAB P200 diffractometer using multi-layer mirror monochromated Cu-Kα radiation (λ = 1.54187 Å). Several copper complexes are too sensitive toward oxygen or moisture to obtain accurate elemental analysis.

Materials: All commercially available reagents and solvents were used as received unless otherwise noted. 1.0 M THF solution of potassium *tert*-butoxide was purchased from Sigma-Aldrich. Benzoyl fluoride was purchased from Tokyo Chemical Industry Co., Ltd. (TCI). DMF was dried over CaH_2. THF, hexane, pentane, C_6D_6, and THF-d_8 were distilled from sodium benzophenone ketyl. The degassed solvents (CH_2Cl_2) used in this work were commercially available. 2-Propanol was dried over K_2CO_3, then CaH_2. CsF, LiF, NaF, KF and CaF_2 were dried by heating at 100 °C for 2 h under reduced pressure. TFE was supplied by Daikin Industries, Ltd.. *N*-Heterocyclic carbenes (NHCs) were synthesized by the known procedures.

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

Preparation of potassium 2-ethylimidazolide (1a•K)

2-ethylimidazole (1.44 g, 15.0 mmol) was added to a round bottom flask equipped with a stirrer bar and dissolved in THF (15.0 mL). 1.0 M THF solution of potassium *tert*-butoxide (15 mL, 15.0 mmol) was added dropwise to the solution. the reaction mixture was stirred at room temperature for 2 hours. After removal of the solvent under reduced pressure, the residual volatiles were further evaporated with hexane. Then, the solid was transferred on a glass filter and washed with hexane (5 mL × 2). The solid was dried under reduced pressure to give potassium 2-ethylimidazolide (**1a•K**) as a white solid in 91% yield (1.83 g, 13.6 mmol).

Preparation of sodium 2-ethylimidazolide (1a•Na)

Sodium *tert*-butoxide (1.44 g, 15.0 mmol) was added to a round bottom flask equipped with a stirrer bar and dissolved in THF (7.0 mL). 2-ethylimidazole (1.44 g, 15.0 mmol) was added to the solution. After the addition of THF (8.0 mL), the reaction mixture was stirred at room temperature for 2 hours. After removal of the solvent under reduced pressure, the residual volatiles were further evaporated with hexane. Then, the solid was transferred on a glass filter and washed with hexane (5 mL × 2). The solid was dried under reduced pressure to give sodium 2-ethylimidazolide (**1a•Na**) as a white solid in 99% yield (1.75 g, 14.8 mmol).

General procedure for preparation of sodium imidazolide derivatives (1b–1e)

Sodium *tert*-butoxide (288 mg, 3.00 mmol) was added to a round bottom flask equipped with a stirrer bar and dissolved in THF (3.0 mL). THF (2.0 mL) solution of imidazole derivative (3.00

mmol) was added dropwise to the flask. After the addition of 3 mL THF, the reaction mixture was stirred at room temperature for 2 hours. After removal of the solvent under reduced pressure, the residual volatiles were further evaporated with hexane (5 mL × 2). Then, the solid was transferred on a glass filter and washed with hexane (5 mL × 2). The solid was dried under reduced pressure to give the corresponding sodium imidazolide. As for **1b** and **1e**, evaporation and filtration were conducted for two times to remove the residual THF.

Optimization of reaction conditions

CuCl (5.0 mg, 0.05 mmol), 0.1 mL DMF solutions of Phen (Phen: 1,10-Phenathroline, 9.0 mg, 0.050 mmol), and 2-ethylimidazolide salt (0.10 mmol) were added to a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7; total volume: 2 mL). Then, α,α,α-trifluorotoluene (as an internal standard, 5.0 μL, 0.042 mmol), DMF (0.2 mL) and C_6D_6 (0.1 mL) were added to the tube. TFE (3.5 atm, > ca. 3.0 equiv.) was then charged into the reactor and the reaction mixture was stored at room temperature for 3 hours. Yields of **2a** and **2a′** were determined by ^{19}F NMR spectra.

Determination of 2a and 2a′

After Phen, CuCl, and two equivalents of potassium 2-ethylimidazolide (**1a•K**) were dissolved in DMF/C_6D_6, a singlet peak of Im–*H* (Im: 2-ethylimidazolyl) and a triplet peak of CH_3– in ethyl group in 2-ethylimidazolide species were observed in ^{1}H NMR spectrum (Figure S1). We consider that it would be due to the generation of [(phen)K][CuIm$_2$]. We have reported a similar reaction in which [(phen)Na][Cu(O^{t}Bu)$_2$] was generated from Phen, CuCl and two equivalents of NaO^{t}Bu.[S1] Subsequently, TFE was pressurized into the reaction mixture. It was speculated that the reaction of [(phen)K][CuIm$_2$] with TFE would have proceeded to furnish [(phen)CuCF$_2$CF$_2$Im] and [(phen)$_2$Cu][Cu(CF$_2$CF$_2$Im)$_2$]. It was speculated that the reaction proceeded in such a manner referring to the reaction in which CuCF$_2$CF$_2$O^{t}Bu and [(DMF)$_2$Cu][Cu(CF$_2$CF$_2$O^{t}Bu)$_2$] were generated from *in situ* generated [(DMF)$_2$Na][Cu(O^{t}Bu)$_2$] and TFE in DMF solution.[S2] In addition, [(phen)CuCF$_2$CF$_2$Im] and [(phen)$_2$Cu][Cu(CF$_2$CF$_2$Im)$_2$] were considered to be **2a** and **2a′** according to a previous report.[S3] We observed two pairs of peaks in the ^{19}F NMR spectra (–94.6/–110.6 and –94.8/–121.9 ppm), which were thought to be **2a** and **2a′**. The intensity of the peak at –94.8 ppm increased relative to that of at –94.6 ppm in the ^{19}F NMR spectra with increasing solvent polarity from DMF (D = 3.86) to DMI (D = 4.09) (40:60 to 45:55) (Figure S2).[S4] Thus, it was speculated that the peak at –94.8 ppm would be the ionic form **2a′** and the peak at –94.6 ppm to be the neutral form **2a**

NMR tube scale one-pot reaction.

Phen (9.0 mg, 0.050 mmol), sodium 2-ethylimidazolide (11.8 mg, 0.0999 mmol), and 4-trifluoromethyl iodobenzene (16.4 mg, 0.0603 mmol) was mixed in DMF (0.2 mL). The mixture was added to CuCl (4.96 mg, 0.0501 mmol). The solution was transferred to a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7; total volume: 2 mL). Then, α,α,α-trifluorotoluene (as an internal standard, 5.0 μL, 0.042 mmol), DMF (0.2 mL) and C_6D_6 (0.1 mL) were added to the tube. TFE (3.5 atm, > ca. 3.0 equiv.) was then charged into the reactor. The reaction mixture was stored at room temperature for 3 hours, then heated at 80 °C for 3 hours. Yields were determined by ^{19}F NMR spectrum.

One-pot synthesis of *N*-fluoroalkyl heteroarenes.

Under N_2 atmosphere, CuCl (49.5 mg, 0.500 mmol) was added to an autoclave reactor (total volume; 50 mL) equipped with a stirrer bar. Then, 1 mL DMF solutions of Phen (90.1 mg, 0.500 mmol), sodium imidazolide derivatives (1.00 mmol), and iodoarene (0.600 mmol) were transferred to the reactor. After the addition of DMF (2 mL), the reactor was capped and TFE (3.5 atm, > ca. 14 equiv.) was charged. After stirring the reaction mixture at room temperature for 3 hours, the reactor was heated at 80 °C for 5 hours with stirring. After remaining TFE was purged from the reactor, the reaction was quenched with ether (10 mL). Following the filtration of the precipitate, the filtrate and water (15 mL) were transferred to a separatory funnel. the resulting mixture was extracted with Et_2O (10 mL × 3). The combined organic phase was dried over $MgSO_4$ and all volatiles were removed under reduced pressure. the crude residue was purified by silica gel column chromatography (hexane/EtOAc = 100:0 to 80:20) to give the corresponding *N*-fluoroalkyl compound **4**.

Compound information.

Potassium 2-ethylimidazolide (1a•K):

^{1}H NMR (400 MHz, DMSO-*d*$_6$, rt, δ/ppm): 6.43 (s, 2H), 2.44 (q, *J* = 7.6 Hz, 2H), 1.10 (t, *J* = 7.6 Hz, 3H). **^{13}C{^{1}H} NMR (100 MHz, DMSO-*d*$_6$, rt, δ/ppm)**: 155.3 (s), 124.0 (s), 25.0 (s), 15.0 (s).

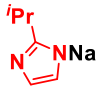
Sodium 2-ethylimidazolide (1a•Na):

^{1}H NMR (400 MHz, DMSO-d_6, rt, δ/ppm): 6.44 (s, 2H), 2.44 (q, J = 7.5 Hz, 2H), 1.10 (t, J = 7.6 Hz, 3H). **^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, rt, δ/ppm)**: 155.4 (s), 124.1 (s), 24.9 (s), 15.0 (s).

Sodium imidazolide (1b•Na): General procedure with imidazole (204 mg, 3.00 mmol) and sodium *tert*-butoxide (288 mg, 3.00 mmol) gave **1b•Na** as a white solid in 84% yield (228 mg, 2.53 mmol).

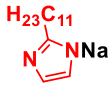
^{1}H NMR (400 MHz, DMSO-d_6, rt, δ/ppm): 7.05 (s, 1H), 6.65 (s, 2H), **^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, rt, δ/ppm): 143.3 (s), 125.0 (s)**.

The analytical data are in agreement with those reported previously.[S5]



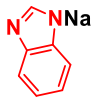
Sodium 2-isopropylidazolide (1c•Na): General procedure with 2-isopropylimidazole (331 mg, 3.00 mmol) and sodium *tert*-butoxide (288 mg, 3.00 mmol) gave **1c** as a white solid in 90% yield (357 mg, 2.70 mmol).

^{1}H NMR (600 MHz, DMSO-d_6, rt, δ/ppm): 6.45 (s, 2H), 2.76 (sept, J = 4.6 Hz, 1H), 1.13 (d, J = 4.0 Hz, 6H). **^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, rt, δ/ppm)**: 159.5 (s), 123.8 (s), 30.2 (s), 23.9 (s).



Sodium 2-undecylimidazolide (1d•Na): General procedure with 2-undecylimidazole (667 mg, 3.00 mmol) and sodium tert-butoxide (288 mg, 3.00 mmol) gave **1d** as a white solid in 90% yield (661 mg, 2.71 mmol).

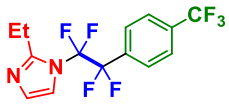
^{1}H NMR (400 MHz, DMSO-d_6, rt, δ/ppm): 6.47 (s, 2H), 2.43 (t, J = 7.4 Hz, 2H), 1.56–1.53 (m, 2H), 1.26 (br, 16H), 0.87 (t, J = 6.0 Hz, 3H). **^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, rt, δ/ppm)**: 154.8 (s), 124.2 (s), 32.3 (s), 31.3 (s), 30.4 (s), 29.7 (s), 29.3 (s), 29.3 (s), 29.2 (s), 29.1 (s), 28.8 (s), 22.1 (s), 13.9 (s).



Sodium benzimidazolide (1e•Na): General procedure with benzimidazole (354 mg, 3.00 mmol)

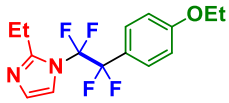
and sodium *tert*-butoxide (288 mg, 3.00 mmol) gave **1e** as a white solid in 87% yield (366 mg, 2.61 mmol).

^{1}H NMR (400 MHz, DMSO-*d*$_6$, rt, δ/ppm): 7.64 (s, 1H), 7.33–7.32 (m, 2H), 6.71–6.69 (m, 2H). **^{13}C{^{1}H} NMR (100 MHz, DMSO-*d*$_6$, rt, δ/ppm)**: 152.7 (s), 146.5 (s), 116.1 (s), 115.9 (s). Chemical shift values in ^{1}H NMR spectrum are slightly deferent from reported values.[S6] It would be because the residual THF and sodium hydroxide was observed in the previous report.



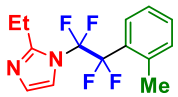
1-(2-ethyl-1*H*-imidazolyl)-2-(*p*-trifluoromethylphenyl)-1,1,2,2-tetrafluoroethane (4aa): General procedure with sodium 2-ethyl imidazolide (**1a•Na**, 118 mg, 0.999 mmol) and 4-trifluoromethyl iodobenzene (**3a**, 163 mg, 0.599 mmol) gave the title compound **4aa** as a yellow oil in 72% yield (122.6 mg, 0.36 mmol).

^{1}H NMR (600 MHz, CDCl$_3$, rt, δ/ppm): 7.74 (d, *J* = 7.8 Hz, 2H), 7.54 (d, *J* = 7.8 Hz, 2H), 6.98 (s, 1H), 6.92 (s, 1H), 2.53 (q, *J* = 7.4 Hz, 2H), 1.25 (t, *J* = 7.5 Hz, 3H). **^{19}F NMR (376 MHz, CDCl$_3$, rt, δ/ppm)**: –65.9 (s, 3F), –97.2 (s, 2F), –115.7 (s, 2F). **^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$, rt, δ/ppm)**: 150.3 (s), 134.1 (q, *J* = 33.0 Hz), 132.5 (t, *J* = 24.8 Hz), 128.4 (s), 127.3 (t, *J* = 6.0 Hz), 125.8 (t, *J* = 3.5 Hz), 123.3 (q, *J* = 271.0 Hz), 117.6 (s), 115.1 (tt, *J* = 255.5, 40.3 Hz), 114.1 (tt, *J* = 266.3, 37.3 Hz), 21.7 (s), 11.8 (s). **HRMS (EI)**: *m/z* $[M]^+$ calcd for $C_{14}H_{11}F_7N_2$: 340.0810; Found: 340.0807.

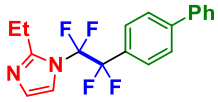


1-(2-ethyl-1*H*-imidazolyl)-2-(*p*-ethoxyphenyl)-1,1,2,2-tetrafluoroethane (4ab): General procedure with sodium 2-ethyl imidazolide (**1a•Na**, 118 mg, 0.999 mmol) and 4-ethoxyiodobenzene (**3b**, 149 mg, 0.601 mmol) gave the title compound **4ab** as a pale yellow oil in 38% yield (60.0 mg, 0.190 mmol).

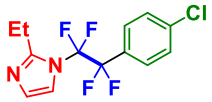
^{1}H NMR (400 MHz, CDCl$_3$, rt, δ/ppm): 7.23 (d, *J* = 8.8 Hz, 2H), 6.94 (s, 1H), 6.90 (d, *J* = 9.2 Hz, 2H), 6.88 (s, 1H), 4.06 (q, *J* = 6.9 Hz, 2H), 2.44 (q, *J* = 7.5 Hz, 2H), 1.43 (t, *J* = 6.8 Hz, 3H), 1.22 (t, *J* = 7.4 Hz, 3H). **^{19}F NMR (376 MHz, CDCl$_3$, rt, δ/ppm)**: –98.1 (t, *J* = 5.6 Hz, 2F), –114.8 (t, *J* = 5.6 Hz, 2F). **^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$, rt, δ/ppm)**: 161.6 (s), 150.3 (s), 128.1 (t, *J* = 6.0 Hz), 127.9 (s),120.3 (t, *J* = 24.8 Hz) 117.7 (s), 116.0 (tt, *J* = 255.0, 38.7 Hz), 114.5 (s), 114.4 (tt, *J* = 267.0, 38.4 Hz), 63.7 (s), 21.5 (t, *J* = 4.5 Hz), 14.6 (s), 11.9 (s). **HRMS (EI)**: *m/z* $[M]^+$ calcd for $C_{15}H_{16}F_4N_2O$: 316.1199; Found: 316.1199.



1-(2-ethyl-1*H*-imidazolyl)-2-(*o*-tolyl)-1,1,2,2-tetrafluoroethane (4ac): General procedure with sodium 2-ethyl imidazolide (**1a•Na**, 118 mg, 0.999 mmol) and *o*-iodotoluene (**3c**, 131 mg, 0.601 mmol) gave the title compound **4ac** as a pale yellow oil in 26% yield (37.5 mg, 0.131 mmol). **^{1}H NMR (600 MHz, $CDCl_3$, rt, δ/ppm)**: 7.40 (ddd, J = 6.6, 4.2, 4.2 Hz, 1H), 7.23 (m, 3H), 6.95 (s, 1H), 6.87 (s, 1H), 2.39 (q, J = 7.4 Hz, 2H), 2.28 (t, J = 3.0 Hz, 3H), 1.20 (t, J = 7.5 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –97.3 (t, J = 5.6 Hz, 2F), –110.8 (t, J = 5.6 Hz, 2F). **^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt, δ/ppm)**: 150.2 (s), 138.0 (t, J = 2.3 Hz), 132.4 (s), 131.7 (s), 128.2 (t, J = 8.3 Hz), 128.0 (s), 126.5 (t, J = 22.5 Hz), 126.0 (s), 117.7 (s), 117.0 (tt, J = 256.5, 39.5 Hz), 114.8 (tt, J = 267.8, 38.0 Hz), 21.4 (t, J = 4.5 Hz), 20.1 (s), 11.8 (s). **HRMS (EI)**: *m/z* $[M]^+$ calcd for $C_{14}H_{14}F_4N_2$: 286.1093; Found: 286.1095.

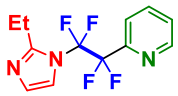


1-(2-ethyl-1*H*-imidazolyl)-2-(*p*-biphenyl)-1,1,2,2-tetrafluoroethane (4ad): General procedure with sodium 2-ethyl imidazolide (**1a•Na**, 118 mg, 0.999 mmol) and 4-iodobiphenyl (**3d**, 168 mg, 0.600 mmol) gave the title compound **4ad** as a white solid in 56% yield (97.8 mg, 0.281 mmol). **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 7.66 (d, J = 8.0 Hz, 2H), 7.59 (d, J = 7.2 Hz, 2H), 7.47 (dd, J = 7.4, 7.4 Hz, 2H), 7.43–7.39 (m, 3H), 6.98 (s, 1H), 6.95 (s, 1H), 2.48 (q, J = 7.5 Hz, 2H), 1.23 (t, J = 7.6 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –97.6 (t, J = 5.6 Hz, 2F), –115.4 (t, J = 5.6 Hz, 2F). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 150.3 (s), 144.9 (s), 139.5 (s), 129.0 (s), 128.3 (s), 128.1 (s), 127.4 (t, J = 24.5 Hz), 127.3 (s), 127.2 (s), 127.0 (t, J = 6.0 Hz), 117.7 (s), 115.8 (tt, J = 255.5, 39.0 Hz), 114.3 (tt, J = 266.5, 37.8 Hz), 21.6 (s), 11.8 (s). **HRMS (EI)**: *m/z* $[M]^+$ calcd for $C_{19}H_{16}F_4N_2$: 348.1250; Found: 348.1251.



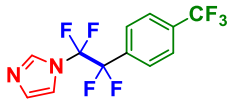
1-(2-ethyl-1*H*-imidazolyl)-2-(4-chlorophenyl)-1,1,2,2-tetrafluoroethane (3be): General procedure with sodium 2-ethyl imidazolide (**1a•Na**, 118 mg, 0.999 mmol) and *p*-chloro iodobenzene (**3e**, 143 mg, 0.600 mmol) gave the title compound **4ae** as a yellow oil in 62% yield (94.7 mg, 0.309 mmol).

^{1}H NMR (600 MHz, $CDCl_3$, rt, δ/ppm): 7.41 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 6.94 (s, 1H), 6.86 (s, 1H), 2.50 (q, *J* = 7.4 Hz, 2H), 1.23 (t, *J* = 7.5 Hz, 3H). **^{19}F NMR (564 MHz, $CDCl_3$, rt, δ/ppm)**: –97.5 (s, 2F), –115.4 (s, 2F). **^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt, δ/ppm)**: 150.2 (s), 138.5 (s), 129.0 (s), 128.2 (s), 128.0 (t, *J* = 6.0 Hz), 127.3 (t, *J* = 24.8 Hz), 117.6 (s), 115.3 (tt, *J* = 255.5, 39.5 Hz), 114.1 (tt, *J* = 266.3, 37.5 Hz), 21.6 (s), 11.8 (s). **HRMS (EI)**: *m/z* $[M]^+$ calcd for $C_{13}H_{11}ClF_4N_2$: 306.0547; Found: 306.0550.



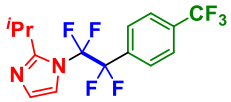
1-(2-ethyl-1*H*-imidazolyl)-2-(2-pyridyl)-1,1,2,2-tetrafluoroethane (4af): General procedure with sodium 2-ethyl imidazolide (**1a•Na**, 118 mg, 0.999 mmol) and 2-iodopyridine (**3f**, 123 mg, 0.600 mmol) gave the title compound **4af** as a yellow oil in 98% yield (134 mg, 0.490 mmol). For the isolation of **4af**, column chromatography was conducted for two times.

^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.72 (d, *J* = 4.4 Hz, 1H), 7.84 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.48 (dd, *J* = 7.6, 4.8 Hz, 1H), 6.96 (s, 1H), 6.95 (s, 1H), 2.60 (q, *J* = 7.6 Hz, 2H), 1.26 (t, *J* = 7.4 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –96.4 (s, 2F), –118.1 (s, 2F). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 150.2 (s), 149.9 (s), 147.8 (t, *J* = 26.0 Hz), 137.2 (s), 128.1 (s), 126.2 (s), 122.2 (t, *J* = 4.5 Hz), 117.5 (s), 114.1 (tt, *J* = 266.5, 36.3 Hz), 113.1 (tt, *J* = 255.5, 39.7 Hz), 21.6 (s), 11.8 (s). **HRMS (EI)**: *m/z* $[M]^+$ calcd for $C_{12}H_{11}F_4N_3$: 273.0889; Found: 273.0890.



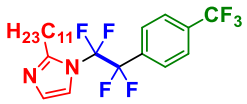
1-(1*H*-imidazolyl)-2-(*p*-trifluoromethylphenyl)-1,1,2,2-tetrafluoroethane (4ba): General procedure with sodium imidazolide (**1b•Na**, 90.1 mg, 1.00 mmol), and 4-trifluoromethyl iodobenzene (**3a**, 163 mg, 0.599 mmol) gave the title compound **3da** as a white solid in 63% yield (98.4 mg, 0.315 mmol).

^{1}H NMR (600 MHz, $CDCl_3$, rt, δ/ppm): 7.71 (d, *J* = 7.8 Hz, 2H), 7.63 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 2H), 7.14 (s, 1H), 7.06 (s, 1H). **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –65.9 (s, 3F), –98.9 (s, 2F), –116.4 (s, 2F). **^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt, δ/ppm)**: 134.9 (s), 134.1 (q, *J* = 33.5 Hz), 132.1 (t *J* = 24.8 Hz), 130.6 (s), 127.2 (t, *J* = 6.0 Hz), 125.8 (q, *J* = 3.5 Hz), 123.2 (q, *J* = 271.0 Hz), 116.5 (s), 114.7 (tt, *J* = 254.3, 39.5 Hz), 113.3 (tt, *J* = 265.5, 37.5 Hz). **HRMS (EI)**: *m/z* $[M]^+$ calcd for $C_{12}H_7F_7N_2$: 312.0497; Found: 312.0496.



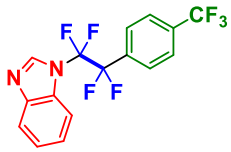
1-(2-isopropyl-1*H*-imidazolyl)-2-(*p*-trifluoromethylphenyl)-1,1,2,2-tetrafluoroethane (4ca): General procedure with sodium 2-isopropyl imidazolide (**1c•Na**, 132 mg, 0.999 mmol), and 4-trifluoromethyl iodobenzene (**3a**, 163 mg, 0.599 mmol) gave the title compound **4ca** as a pale yellow oil in 68% yield (120 mg, 0.339 mmol).

^{1}H NMR (600 MHz, $CDCl_3$, rt, δ/ppm): 7.71 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 7.8 Hz, 2H), 6.97 (s, 1H), 6.85 (s, 1H), 2.72 (sept, J = 6.7 Hz, 1H), 1.18 (d, J = 6.6 Hz, 6H). **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –65.9 (s, 3F), –96.6 (s, 2F), –115.9 (s, 2F). **^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt, δ/ppm)**: 154.6 (s), 134.1 (q, J = 32.5 Hz), 132.5 (t J = 24.8 Hz), 128.4 (s), 127.2 (t, J = 6.0 Hz), 125.8 (q, J = 3.5 Hz), 123.3 (q, J = 271.0 Hz), 116.9 (s), 115.0 (tt, J = 255.8, 40.0 Hz), 114.1 (tt, J = 266.3, 36.8 Hz), 27.8 (s), 22.2 (s). **HRMS (EI)**: *m/z* $[M]^+$ calcd for $C_{15}H_{13}F_7N_2$: 354.0967; Found: 354.0964.



1-(2-undecyl-1*H*-imidazolyl)-2-(*p*-trifluoromethylphenyl)-1,1,2,2-tetrafluoroethane (4da): General procedure with sodium 2-undecylimidazolide (**1d•Na**, 244 mg, 0.999 mmol) and 4-trifluoromethyl iodobenzene (**3a**, 163 mg, 0.599 mmol) gave the crude material including **4da**. Further purification by HPLC gave **4da** as a white solid in 51% yield (118 mg, 0.253 mmol).

^{1}H NMR (600 MHz, $CDCl_3$, rt, δ/ppm): 7.72 (d, J = 7.8 Hz, 2H), 7.52 (d, J = 7.8 Hz, 2H), 6.96 (s, 1H), 6.90 (s, 1H), 2.43 (t, J = 7.5 Hz, 2H), 1.69–1.64 (m, 2H), 1.28–1.24 (m, 16H), 0.86 (t, J = 6.9 Hz, 3H). **^{19}F NMR (564 MHz, $CDCl_3$, rt, δ/ppm)**: –65.9 (s, 3F), –97.0 (s, 2F), –115.7 (s, 2F). **^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt, δ/ppm)**: 149.4 (s), 134.1 (q, J = 33.0 Hz), 132.5 (t J = 24.8 Hz), 128.4 (s), 127.3 (t, J = 6.8 Hz), 125.8 (q, J = 3.5 Hz), 123.3 (q, J = 271.0 Hz), 117.4 (s), 115.1 (tt, J = 255.8, 39.8 Hz), 114.1 (tt, J = 265.5, 37.0 Hz), 31.9 (s), 29.6 (s), 29.5 (s), 29.3 (s), 29.3 (s), 29.3 (s), 28.3 (m), 27.6 (s), 22.6 (s), 14.0 (s). **HRMS (EI)**: *m/z* $[M]^+$ calcd for $C_{23}H_{29}F_7N_2$: 466.2219; Found: 466.2215.



1-(1*H*-benzimidazolyl)-2-(*p*-trifluoromethylphenyl)-1,1,2,2-tetrafluoroethane (4ea): General

procedure with sodium benzimidazolide (**1e•Na**, 140 mg, 0.999 mmol) and 4-trifluoromethyl iodobenzene (**3a**, 163 mg, 0.599 mmol) gave the title compound gave the title compound **4ea** as a white solid in 61% yield (110 mg, 0.304 mmol).

^{1}H NMR (600 MHz, $CDCl_3$, rt, δ/ppm): 7.90 (s, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H). **^{19}F NMR (564 MHz, $CDCl_3$, rt, δ/ppm)**: –65.9 (s, 3F), –98.8 (s, 2F), –115.7 (s, 2F). **^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, rt, δ/ppm)**: 143.4 (s), 139.3 (s), 134.2 (q, *J* = 33.0 Hz), 132.2 (t, *J* = 24.0 Hz), 131.5 (s), 127.3 (t, *J* = 6.0 Hz), 125.8 (q, *J* = 3.5 Hz), 125.0 (s), 124.1 (s), 123.3 (q, *J* = 271.0 Hz), 121.0 (s), 115.4 (tt, *J* = 255.0, 40.5 Hz), 114.4 (tt, *J* = 266.3, 37.8 Hz), 112.1 (s). **HRMS (EI)**: *m/z* $[M]^+$ calcd for $C_{16}H_9F_7N_2$: 362.0654; Found: 362.0661.

2.9. References of experimental section

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S2. M. Ohashi, T. Adachi, N. Ishida, K. Kikushima, S. Ogoshi, *Angew. Chem. Int. Ed.* **2017**, *56*, 11911.

S3. H. Morimoto, T. Tsubogo, N. D. Litvinas, J. F. Hartwig, *Angew. Chem., Int. Ed.* **2011**, *50*, 3793.

S4. J. R. Langan, K. J. Liu, G. A. Salmon, P. P. Edwards, A. Ellaboudy, D. M. Holton, *Proc. R. Soc. Lond. A.* **1989**, *421*, 169.

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S6. M. S. Shannon, M. S. Hindman, S. P. O. Danielsen, J. M. Tedstone, R. D. Gilmore, J. E. Bara, *Sci. China Chem.* **2012**, *55*, 1638.

Chapter 3

Cu(I)-Catalyzed Pentafluoroethylation of Iodoarenes via Fluorocupration of Tetrafluoroethylene

3.1 Introduction

Trifluoromethylated aryl compounds (Ar–CF_3) are one of the most attractive structural motifs in biologically active compounds since the trifluoromethyl group can provide unique key properties, such as high lipophilicity, metabolic stability, and strong electron-withdrawing ability.[1] In fact, both fluorinated and trifluoromethylated aromatic compounds accounted for a major portion of 136 new fluorine-containing drugs whicave been brought to market between 1991 to 2016.[2] On the other hand, no pentafluoroethylated aryl compounds (Ar–C_2F_5) was found in the new drug list, while few biologically-active compounds containing the pentafluoroethyl group, as shown in the angiotensin II receptor antagonist (DuP 532) and antihypertensive K^+ channel opener (KC-515), have been reported to date (Figure 3.1).[3]

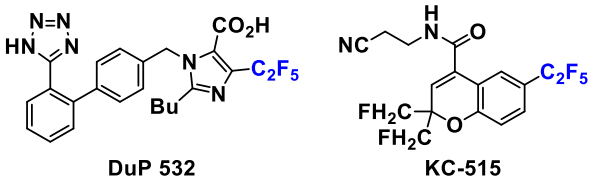


Figure 3.1. Pentafluoroethylated bioactive aromatic compounds

Therefore, the development of practical and reliable pentafluoroethylations of aromatic compounds is highly desirable. Since trifluoromethyl copper(I) species (Cu–CF_3) have played a key important role in the trifluoromethylation reactions of the aromatic compounds,[4] one of few practical methods for introducing a pentafluoroethyl group into the aromatic ring is cross-coupling reactions of pentafluoroethyl copper(I) species (Cu–C_2F_5) with aryl halides.[4a,n,q,v,w,5] However, in comparison with the trifluoromethylation reactions, the introduction of a long-chain perfluoroalkyl group into aromatic compounds remains largely unexplored. The generation of Cu–C_2F_5 key

intermediate are roughly divided into three routes (Figure 3.2): (1) via the transmetalation of pentafluoroethyl anion equivalent with copper salt,[4a,v,w,5a,b] (2) via the deprotonation of pentafluoroethane (C_2F_5H),[4q,5c,6] and (3) via reaction with pentafluoroethylpropionate derivatives.[4n,7]

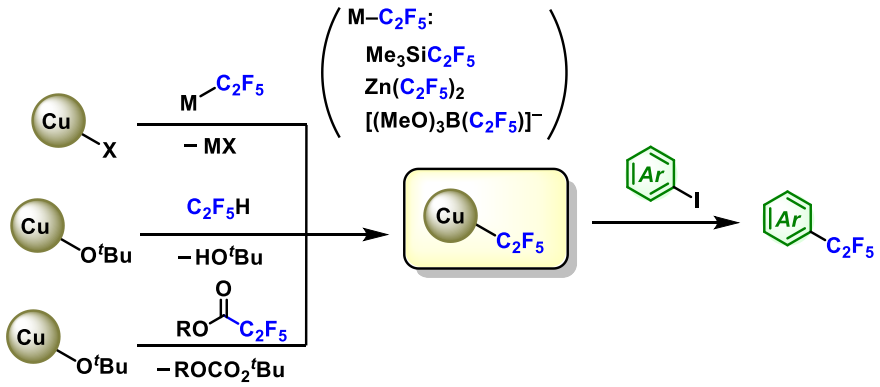
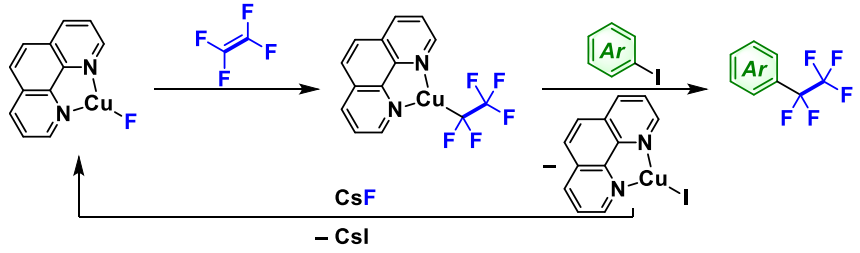


Figure 3.2. Synthesis and reaction of pentafluoroethyl copper complex

As literated in Chapter 1 and 2, we have investigated the addition of metal species to TFE. Thus, we envisioned that copper fluoride complex would add to TFE to give the corresponding pentafluoroethyl copper complex. In 2017, Hu reported a similar reaction in which pentafuoroethyl copper complex was generated in situ from Phen, CuCl, CsF and TFE. However, the reaction mechanism was not studied and only stoichiometric reaction was conducted.[8]

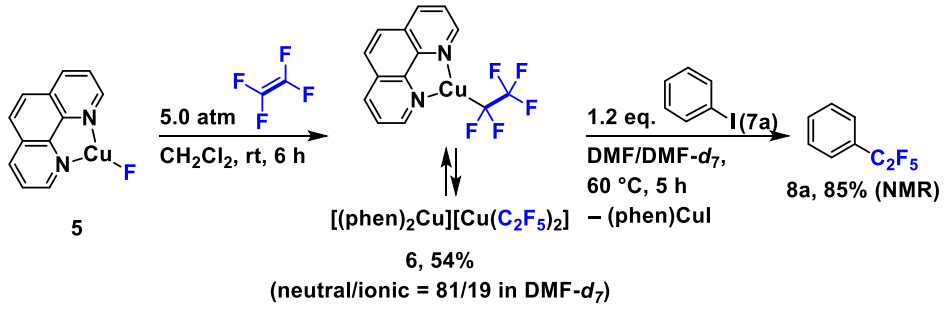
Described in this Chapter is a copper-catalyzed pentafluoroethylation of iodoarenes. In this reaction, it was revealed that copper(I) fluoride can add to TFE to give pentafluoroethyl copper species. In addition, when the reaction was conducted in the presence of fluoride anion, the reaction proceeded catalytically.



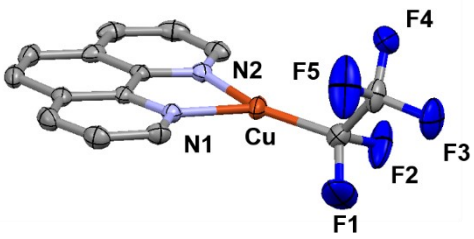
Scheme 3.1. Copper-catalyzed pentafluoroethylation of iodoarenes using TFE

3.2 Preparation of (phen)CuC_2F_5 by fluorocupration of TFE

Exposure of a CH_2Cl_2 solution of (phen)CuF (**5**) to 5.0 atm of TFE at room temperature for 6 h underwent the desire fluorocupration to yield (phen)CuC_2F_5 (**6**) in 54% isolated yield as an orange solid (Scheme 3.2). The structure of **6** was unambiguously determined by single crystal X-ray diffraction analysis (Figure 3.3). In DMF-d_7, **6** showed an equilibrium bitween a neutral form and an inoic form, as shown in Chapter 1 and 2.[9] In agreement with the report by Hu,[8] treatment of the isolated **6** with iodobenzene (**7a**) in DMF/DMF-d_7 at 60 ºC yielded pentafluoroethyl benzene (**8a**) in 85% yield (Scheme 3.2).



Scheme 3.2. Synthesis and reaction of pentafluoroethyl copper **6**



C2/c
R_1 = 0.0398
wR_2 = 0.1104

Figure 3.3. ORTEP drawing of (phen)CuC_2F_5 (**6**) with thermal ellipsoids at the 30% probability level. H atoms have been omitted for clarity.

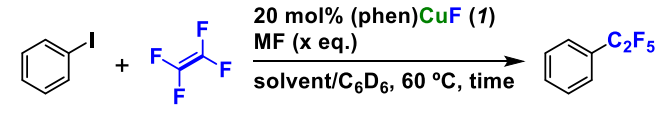
3.3 Optimization of reaction conditions for catalytic pentafluoroethylation of iodoarenes

A DMF/C_6D_6 (v/v'=4/1) solution of **7a** (0.10 mmol in 0.4 mL solvent; total volume of the pressure-tight NMR tube: 2.0 mL) was exposed to TFE (5.0 atm, c.a. > 3 equiv.) in the presence of a catalytic amount of (phen)CuF (**5**, 20 mol%) and a fluoride source and heated at 60 °C. When KF or CsF was used as a fluoride source, the desired **8a** was furnished in 31%, and 50% yield, respectivelu (Table 1, entries 1, 2). Therefore, CsF was

determined as the best F^- source. Then, the solvent effect was further investigated: using DMA or NMP afforded **8a** in 41% and 64% yield, respectively (entries 3, 4), indicating that DMF and NMP were suitable for the reaction. Increasing the loading of CsF to 3 equiv. with respect to **7a** resulted in an improvement of the yield of **8a** to about 80% (entries 5, 6). (phen)CuF **5**, was crucial; otherwise pentafluoroethylation did not proceed (entry 7). This result clearly showed that copper species is the key intermediate for facilitating the catalytic pentafluoroethylation. In a nod to the cost of the solvent used, DMF was chosen as the optimal solvent.

In response to the result of the stoichiometric reaction, our efforts were devoted to the development of the Cu(I)-catalyzed pentafluoroethylation of iodoarenes in the presence of metal fluoride as a fluoride anion source.

Table 3.1. Optimization of reaction conditions



7a 0.10 mmol | 5.0 atm >3.0 eq. | *8a*

entry	MF (x eq.)	solvent	time / h	yield / %[a]
1	KF (1.0)	DMF	63	31
2[b]	CsF (1.0)	DMF	63	50
3	CsF (1.0)	DMA	55	41
4	CsF (1.0)	NMP	65	64
5	CsF (3.0)	DMF	68	81
6	CsF (3.0)	NMP	87	80
7[c]	CsF (3.0)	DMF	55	n.d.

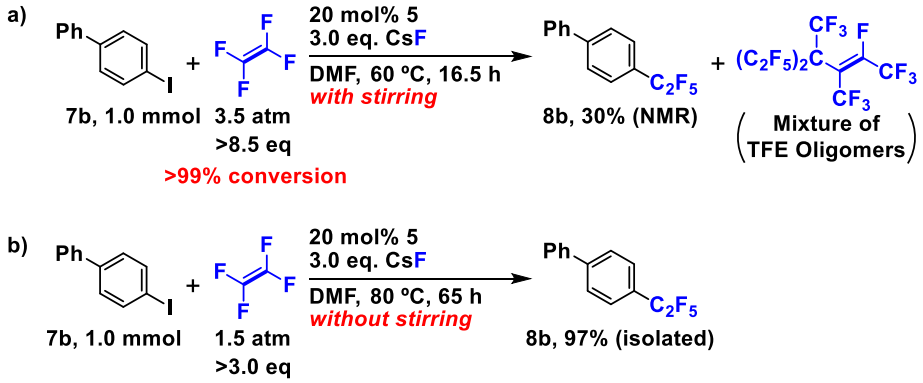
[a] Yield was determined by ^{19}F NMR. [b] 0.15 mmol PhI, 3.5 atm (>2.0 eq.) were used. [c] Without (phen)CuF.

3.4 Scale up reaction using an autoclave reactor

With the optimal reaction conditions in hand, the catalytic reaction was conducted on a larger scale (1.0 mmol of 4-iodobiphenyl (**7b**)) using a 50 mL autoclave reactor. In the presence of 20 mol% (phen)CuF, and 3 equiv. of CsF, DMF solution of 4-iodobiphenyl **7b** was heated at 60 °C for 16.5 h with stirring, which resulted a diminished yield of 4-pentafluoroethybiphenyl (**8b**, 30%) and considerable oligomerization of TFE (Scheme 3.3a). In this reaction, all of TFE was consumed and the major component of the resultant oligomer was the pentamer. Graham reported that a similar oligomerization of TFE in

diglyme solution was facilitated by the addition of CsF,[10] and such an oligomerization was confirmed to take place indeed by treating a DMF solution of CsF with TFE in the autoclave reactor with stirring. Cooling down of the reaction mixture to room temperature caused phase separation between an organic (DMF) layer and a fluorous layer that consisted of the resultant oligomer.

Based on the fact that the oligomer was not generated in the tube-scale reaction, the reaction was carried out without stirring to suppress the undesired oligomerization of TFE, thus leading to the isolation of **8b** in 97% yield (Scheme 3.3b). The undesired oligomerization was inhibited under the unstirred reaction conditions, clearly indicating that the dissolved concentration of TFE in DMF solution is the key factor for suppressing oligomerization of TFE. However, both elongation of the reaction time as well as elevation of the reaction temperature, were required for facilitating the desired pentafluoroethylation in high product yield, since enhancement of the product selectivity by decreasing the dissolved concentration of TFE inevitably caused a decline in the efficiency of the reaction.

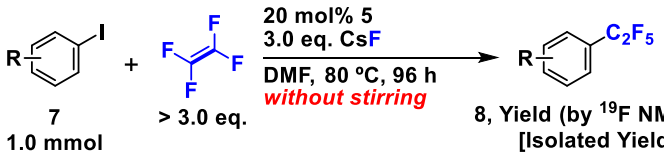


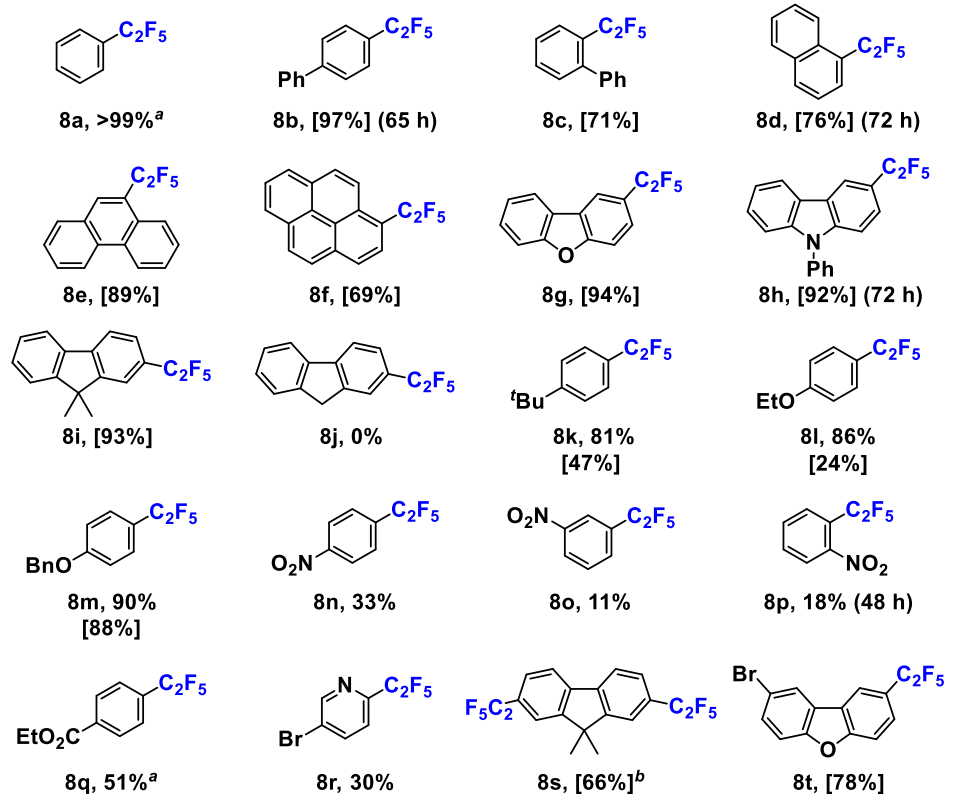
Scheme 3.3. Scale-up reaction using an autoclave reactor

3.5 Substrate Scope

The scope and limitations in the Cu(I)-catalyzed pentafluoroethylation was investigated (Table 3.2). When iodobenzene (**7a)** was employed, the reaction proceeded quantitatively, affording **8a**, albeit its isolation was hampered by its high volatility. Next, substrates with relatively-higher molecular weight were investigated. This catalytic reaction could be applied to polycyclic iodoarenes: the reaction with monoiodobiphenyl derivatives (**7b**,**c**) allowed us to isolate the corresponding pentafluoroethylated products (**8b**,**c**) in good to excellent yields (**8b**: 97%, **8c**: 71%). The reaction with 1-iodonaphtharene (**7d**) furnished 1-pentafluoroethylnaphtharene (**8d**) in 76% yield. 9-Iodophenanthrene (7e) and 1-iodopyrene (7f) also yielded the corresponding products (8e,f) in good to excellent yield (8e: 89%, 8f: 69%). Furthermore, the use of 2-iododibenzofuran *(7**g**), N*-phenyl-3-iodocarbazole *(7**h**) and 2-iodo-9,9-dimethyl*-fluorene *(7**i**) led to the almost quantitative formation of the corresponding products (**8g**: 94%, 8**h**: 92%, **8i**: 93%).* However, using 2-iodofluorene (**7j**), which contains weakly acidic protons (pK_a = 22.6 in DMSO[11]) at the C9 position, did not afford the expected 2-pentafluoroethylfluorene (**8j**). Further we then further investigated the electronic influence of the ring substituents in monoaromatic compounds on the catalytic activity. The use of electron-rich aryl iodides, such as *p-tert*-butyl- (**7k**), *p*-ethoxy- (**7l**), and *p*-benzyloxy- iodoarene (**7m**), afforded the corresponding products (**8k–m**) in excellent yields, although the isolated yields of **8k** and **8l** were dramatically decreased compared to their NMR yields due to their high volatility. On the other hand, the reaction with iodoarene bearing a nitro group (**7n–p**) retarded the catalytic reaction, whereas stoichiometric treatment of **7n–p** with **6** resulted in the clean formation of the corresponding product.[8] In addition, the reactions with *p*-iodo ethylbenzoate (**7q**) and *o*-iodo pyridine derivative (**7r**) were sluggish. *Moreover, diiodoarene (7**s**)* were used with 40 mol% (phen)CuF, bispentafluoroethylated products were given as a major product. When 2-bromo-8-iododibenzofuran (**7t**) was employed, 2-bromo-8-(pentafluoroethyl)dibenzofuran (**8t**) was obtained as the major product, albeit that trace amount of 4s were also detected due to a pentafluoroethylation of the C(sp^2)–Br bond.

Table 3.3. Substrate Scope

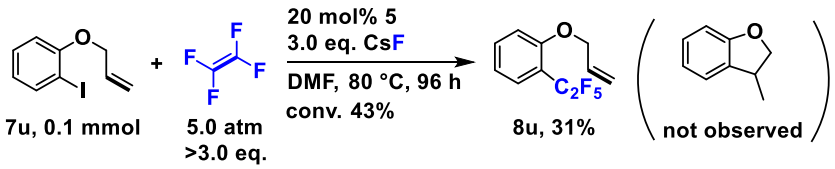




[a]Conducted at 0.1 mmol scale. [b]40 mol% (phen)CuF was used.

3.6 Reaction with 1-allyloxy-2-iodobenzene

When 1-allyloxy-2-iodobenzene (**7u**) was employed in the catalytic pentafluoroethylation, 1-allyloxy-2-pentafluoroethylbenzene (**8u**) was obtained in 31% isolated yield (in 41% NMR yield found in the crude reaction mixture). In the crude products, 3-methyl-2,3-dihydrobenzofuran, which should be generated if the pentafluoroethylation takes place via an aryl radical intermediate, was not detected by GC/MS analysis. This result indicated that the aryl radical intermediate was not involved in the copper-catalyzed pentafluoroethylation.



Scheme 3.4. Reaction using 1-allyloxy-2-iodobenzene

3.7 Monitoring of the reaction of (phen)CuI with excess amount of CsF:

Since no ^{19}F resonance appears in the ^{19}F NMR spectrum of (phen)CuF (**5**) measured at room temperature, the regeneration reaction from (phen)CuI to **5** was monitored by means of UV-vis spectroscopy (Figure 3.4). When the solution of (phen)CuI and CsF was heated at 80 °C for 3 h, the UV-Vis spectrum of the solution was close to that of **5**. Therefore, considered that 5 was generated in the reaction of (phen)CuI and CsF.

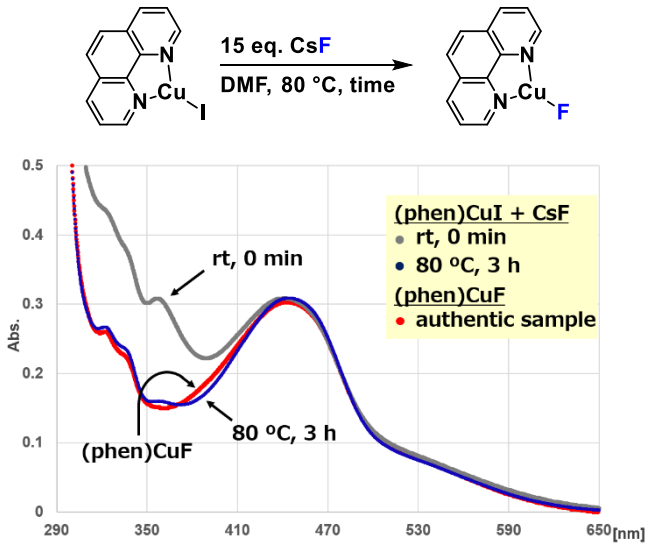
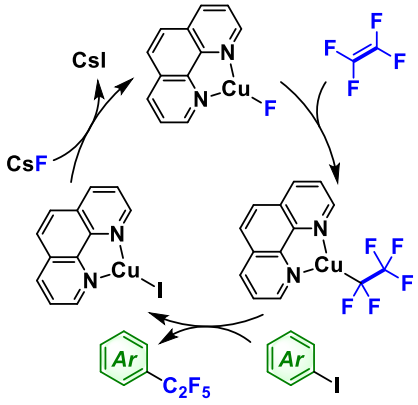


Figure 3.4. UV-vis absorbance monitoring the reaction of (phen)CuI with CsF

3.8 Plausible reaction mechanism

We consider that this reaction proceeds as below (Scheme 3.5). Fluorocupration of TFE and coupling reaction of **6** with iodoarenes were confirmed by a stoichiometric reaction in Scheme 3.2. Transmetalation of (phen)CuI with CsF was confirmed by. UV-Vis measurement in Figure 3.4. Another possible route leading to the key intermediate **6**, in which (phen)CuI directly undergoes a transmetalation with CsC_2F_5,[12] cannot be ruled out completely, given that the competing oligomerization of TFE occurred, which suggests the generation of CsC_2F_5 *in situ* (Scheme 3.3a).[13]



Scheme 3.5. A plausible reaction mechanism

3.9 Conclusion

In Chapter 3, the synthesis, characterization, and synthetic application of pentafluoroethyl copper complexes, which are generated by the fluorocupration of TFE were demonstrated. The molecular structure was unambiguously determined by X-ray crystallography and NMR analysis. Using the complex as a pentafluoroethylation catalyst, we synthesized a variety of pentafluoroethyl arenes in high yield. In this reaction, it was important to conduct the reaction without stirring to proceed the pentafluoroethylation efficiently.

3.10 References and notes

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3.11 Experimental section

Preparation of (phen)CuF (5)[S1]

To a mixture of CuO^{t}Bu (820 mg, 6.0 mmol) and 1,10-phenanthroline (phen; 1.08 g, 6.0 mmol) was added THF (10.0 mL), and then the resultant reddish-brown solution was stirred for 1.5 h at room temperature. Benzoyl fluoride (894 mg, 7.2 mmol) was then added to the solution, leading to the immediate precipitation of purple solid. The reaction mixture was further stirred for 10 min, and all volatiles were then removed *in vacuo*. The residue was washed with pentane (10 mL x 3) and dried under reduced pressure, affording (phen)CuF (**5**; 1.52 g, 96%) as a purple powder. ^{1}H NMR (400 MHz, DMF-d_7, rt, δ/ppm): 9.20 (br s, 2H), 8.96 (br s, 2H), 8.40 (br s, 2H), 8.13 (br s, 2H).

Preparation of (phen)CuC$_2$F$_5$ (6)

A CH_2Cl_2 solution (2.5 mL) of **5** (52.4 mg, 0.20 mmol) was transferred into an autoclave reactor (total volume: 50.0 mL), and TFE (5.0 atm) was then charged into the reactor. The reaction mixture was left to stand at room temperature for 6 h, leading to the gradual precipitation of reddish-orange microcrystalline solid. After any excess of TFE was purged from the reactor, supernatant was removed by decantation. The residue washed with pentane and dried under reduced pressure, yielding the title compound (**6**; 39.4 mg, 54%) as an orange microcrystalline solid. Single crystals for X-ray diffraction analysis were prepared by recrystallization from

CH_2Cl_2 at room temperature. Spectral data for **6**: **^{1}H NMR (400 MHz, DMF-d_7, rt, δ/ppm)**: 9.21 (br s, 2H), 8.96 (br s, 2H), 8.38 (br s, 2H), 8.14 (br s, 2H). **^{13}C{1H} NMR (100 MHz, DMF-d_7, rt, δ/ppm)**: 127.0 (s), 128.3 (s), 130.6 (s), 138.5 (s), 144.8 (s), 150.9 (s). The resonances assignable to the CF_2CF_3 moiety were not distinctly observed due to their multiple coupling. ^{19}F NMR analysis revealed that, in DMF solution, **6** exists as an equilibrium mixture of a neutral form ([(phen)Cu(C_2F_5)]; **6**neutral) and an ionic form ([(phen)$_2$Cu][Cu(C_2F_5)$_2$]; **6**ionic). Spectral data for **6**neutral: **^{19}F NMR (376 MHz, DMF-d_7, rt, δ/ppm)**: –87.8 (s, 3F), –120.1 (s, 2F). Spectral data for **6**ionic: **^{19}F NMR (376 MHz, DMF-d_7, rt, δ/ppm)**: –87.8 (s, 3F), –112.3 (s, 2F). Anal. Calcd. for $C_{14}H_8CuF_5N_2$: C, 46.35; H, 2.22; N, 7.72; Found: C, 45.51; H, 2,47; N, 7.43. X-ray data for **6**: M = 362.76, yellow, monoclinic, C2/c (No, 15), a = 19.8936(3) Å, b = 6.65450(10) Å, c = 21.0135(3) Å, β = 109.5046(17) °, V = 2622.17(7) Å ^{3}, Z = 8, D_{calcd} = 1.838g/cm^{-3}, T = –150(2) °C, R_1 (wR_2) = 0.0398 (0.1087).

Preparation of (phen)CuI [S2]

To a mixture of CuI (85.8 mg, 0.5 mmol) and Phen (90.9 mg, 0.5 mmol) was added THF (4.0 mL), leading to the gradual precipitation of purple solid. The reaction mixture was stirred for 1 h at room temperature, and all volatiles were then removed *in vacuo*. The residue was washed with THF (5 mL × 3) and hexane (5 mL × 3) dried under reduced pressure, affording (phen)CuI (131.5 mg, 71%) as an oragne solid.

Reaction of (phen)CuC_2F_5 (6) with iodobenzene

A DMF/DMF-d_7 solution (0.50 mL, v/v' = 4/1) of **6** (7.3 mg, 0.02 mmol), iodobenzene (7a; 2.6 μL, 4.8 mg, 0.024 mmol), and α,α,α-trifluorotoluene (5.0 μL, as an internal standard) was transferred into an NMR tube equipped with a J-Young valve. The reaction mixture was heated at 60 °C for 5 h. ^{19}F NMR analysis revealed the formation of pentafluoroethylbenzene (**8a**) in 85% yield.

Optimization of the reaction conditions for the Cu(I)-catalyzed pentafluoroethylation of 7a in the presence of TFE and metal fluoride as a source of fluoride anions.

Each catalytic reaction was conducted in a pressure-tight NMR tube (Wilmad-LabGlass 524-PV-7; total volume: 2.0 mL). The yield of **8a** was determined by ^{19}F NMR analysis using α,α,α-

trifluorotoluene as an internal standard.

The evaluation of metal fluoride as a source of fluoride anions (Table 4.1; Runs 1 and 2):

To a DMF/C_6D_6 suspension (0.5 mL, v/v' = 4/1) of **5** (5.3 mg, 0.02 mmol), **7a** (10.8 μL, 20.0 mg, 0.10 mmol), metal fluoride (CsF or KF; 0.10 mmol) was added α,α,α-trifluorotoluene (5.0 μL, as an internal standard). The suspension was transferred into a pressure-tight NMR tube. TFE (5.0 atm, c.a. > 0.30 mmol) was then charged into the tube, and the reaction mixture was heated at 60 °C. Monitoring the reaction by ^{19}F NMR spectroscopy revealed that the catalytic reaction was found to terminate after 63 h.

The evaluation of the solvent (Table 3.1.; Runs 3–4):

To a given suspension (0.5 mL, solvent/C_6D_6 = 4/1) of **5** (5.3 mg, 0.02 mmol), **7a** (10.8 μL, 20.0 mg, 0.10 mmol), CsF (15.2 mg, 0.10 mmol) was added α,α,α-trifluorotoluene (5.0 μL, as an internal standard). The suspension was transferred into a pressure-tight NMR tube. TFE (5.0 atm, c.a. > 0.30 mmol) was then charged into the tube, and each reaction mixture was heated at 60 °C until the catalytic reaction was found to terminate.

The evaluation of the amount of CsF (Table 3.1.; Runs 5–6):

To a given suspension (0.5 mL, DMF or NMP/C6D6 = 4/1) of **5** (5.3 mg, 0.02 mmol), **7a** (10.8 μL, 20.0 mg, 0.10 mmol), CsF (45.6 mg, 0.30 mmol) was added α,α,α-trifluorotoluene (5.0 μL, as an internal standard). The suspension was transferred into a pressure-tight NMR tube. TFE (5.0 atm, c.a. > 0.30 mmol) was then charged into the tube, and each reaction mixture was heated at 60 °C until the catalytic reaction was found to terminate.

Control experiment in the absence of 1 (Table S1; Run 7):

To a DMF/C_6D_6 suspension (0.5 mL, v/v' = 4/1) of 3a (10.8 μL, 20.0 mg, 0.10 mmol), CsF (45.6 mg, 0.30 mmol) was added α,α,α-trifluorotoluene (5.0 μL, as an internal standard). The suspension was transferred into a pressure-tight NMR tube. TFE (5.0 atm, c.a. > 0.30 mmol) was then charged into the tube, and each reaction mixture was heated at 60 °C for 55 h. ^{19}F NMR analysis revealed no formation of **8a**.

General Procedure for the Cu(I)-Catalyzed pentafluoroethylation of aryl iodides

To a mixture of (phen)CuF (52.5 mg, 0.20 mmol), iodoarenes (1.00 mmol), and CsF (456 mg, 3.00 mmol) was added DMF (5.0 mL). The resulting solution was transferred into an autoclave reactor, and then TFE (1.5 atm, c.a. > 3.0 mmol) was charged into the reactor. The reaction mixture was thermostated at 80 ºC for 96 h without stirring. After the unreacted TFE was purged from the reactor, the reaction mixture was quenched with deionized water (40 mL). Aqueous phase was extracted with Et_2O (40 mL × 5). Combined organic phase was further washed with water (40 mL × 3), and then dried over Na_2SO_4. All volatiles were removed under reduced pressure. Purification by silica gel column chromatography gave the corresponding pentafluoroethylated compounds.

Cu(I)-catalyzed pentafluoroethylation of 3b in the presence of TFE and CsF (Scheme 3.3) (The reaction was conducted in a 50 mL glass autoclave reactor with stirring):

A DMF suspension (5.0 mL) of **5** (52.5 mg, 0.20 mmol), 4-iodobiphenyl (**7b**; 281 mg, 1.00 mmol), CsF (456 mg, 3.00 mmol) was transferred into the autoclave reactor. TFE (1.5 atm, c.a. > 3.0 mmol) was then charged into the reactor. The reaction mixture was thermostated at 60 ºC with stirring, and a pressure gauge attached to the reactor indicated that all of TFE was consume completely after 16.5 hours of stirring. The crude reaction mixture was found to be phase-separating into the organic (DMF) and fluorous layers. ^{19}F NMR analysis, using α,α,α-trifluorotoluene as an internal standard, of the DMF layer revealed that **8b** was obtained in 30% yield. The fluorous layer consisted of a mixture of TFE oligomers, whereby the major component of the resulting oligomer mixture was the pentamer (See also the control experiment described below). The yield of the pentamer could not be estimated from ^{19}F NMR analysis due to its insolubility in any organic solvents.

CsF-mediated oligomerization of tetrafluoroethylene in DMF solution:

This reaction was conducted in a 200 mL glass autoclave reactor. A DMF suspension (5.0 mL) of CsF (456 mg, 3.00 mmol) was transferred into the autoclave reactor. TFE (3.5 atm, c.a. > 30.0 mmol) was then charged into the reactor. The reaction mixture was thermostated at 60 ºC with stirring, and a pressure gauge attached to the reactor indicated that all of TFE was consume completely after 30 hours of stirring. The crude reaction mixture was found to be phase-separating into the organic (DMF) and fluorous layers. The fluorous layer was purified by KugelRohr

distillation to yield the pentamer (2.27 g, 4.54 mmol). The neat pentamer was transferred into an NMR tube, and a capillary filled with C_6D_6 was then added to the NMR tube as an external standard. **^{19}F NMR (376 MHz, neat, rt, δ/ppm)**: –52.9 (s, 3F), –58.5 (s, 3F,), –68.8 (q, 3F), –76.3 (m, 1F), –80.4 (m, 6F), –106.8 (m, 4F). **^{13}C{^{19}F} NMR (150 MHz, neat, rt, δ/ppm)**: 63.7 (-$C(C_2F_5)_2(CF_3)$), 109.1 (C=$CFCF_3$), 114.1 (–CF_2–), 117.5 (–CF_3), 118.1 (–CF_2CF_3), 120.6 (–CF_3), 120.7 (–CF_3), 159.4 (=$CFCF_3$).

Preparation of 1-allyloxy-2-iodobenzene (7u)[S3]:

To a DMF suspension (10.0 mL) of 2-iodophenol (1.18 g, 5.37 mmol) and K_2CO_3 (1.49 g, 11.6 mmol) was added allyl bromide (550 μL, 713 mg, 5.89 mmol). The reaction mixture was stirred at 60 °C for 24 h. The reaction mixture was poured into deionized water (10 mL), and the resultant mixture was extracted with Et_2O (10 mL × 5). Combined organic phase was further washed with brine (10 mL), and then dried over anhydrous $MgSO_4$. All volatiles were removed under reduced pressure, and the crude product was further purified by silica gel column chromatography (eluate: hexane), affording **7u** (1.35 g, 96%) as colorless oil. 1H NMR (400 MHz, C_6D_6, rt, δ/ppm): 4.00 (dt, *J* = 4.6, 2.0 Hz, 2H), 5.03 (d, *J* = 10.8 Hz 1H), 5.34 (d, *J* = 17.3 Hz, 1H), 5.70 (m, 1H), 6.30 (d, *J* = 8.3 Hz, 1H), 6.39 (tt, *J* = 7.5, 1.1 Hz, 1H), 6.92 (tt, *J* = 7.8, 1.2 Hz, 1H), 7.67 (dd, *J* = 7.8, 1.4 Hz, 1H).

Substrate scope in the Cu(I)-catalyzed pentafluoroethylation of iodoarenes (7) in the presence of TFE and CsF.

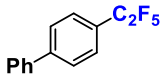
General procedure A (for isolation of the product):

Each catalytic reaction for isolation of the product was conducted in a 50 mL glass autoclave reactor. A DMF suspension (5.0 mL) of **5** (52.5 mg, 0.20 mmol), iodoarenes (**7**; 1.00 mmol), CsF (456 mg, 3.00 mmol) was transferred into the autoclave reactor. TFE (1.5 atm, c.a. > 3.0 mmol) was then charged into the reactor. The reaction mixture was thermostated at 80 ºC for 96 h without stirring. After any excess of TFE was purged from the reactor, the reaction mixture was quenched with deionized water (40 mL). Aqueous phase was extracted with Et_2O (40 mL × 5). Combined organic phase was further washed with water (40 mL × 3), and then dried over anhydrous Na_2SO_4. All volatiles were removed under reduced pressure, and the crude product was further purified by silica gel column chromatography, affording the title compound **8**. For products **8o–r**, isolation

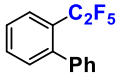
of each reaction product was hampered by its relatively-lower yield as well as its high volatility. Spectral data for the isolated compounds **8b**, **8d**, and **8h** showed good agreement with the literature data.[S4] As for these compounds **8b**, **8d**, and **8h**, we present only NMR data in this section.

General procedure B (for the evaluation of substrate scope):

When either iodobenzene (**7a**) or ethyl *p*-iodobenzoate (**8n**) was employed as the substrate, each catalytic reaction was conducted in a pressure-tight NMR tube (Wilmad-LabGlass 524-PV-7; total volume: 2.0 mL). The yield of **8** in the crude product was estimated by ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard. To a DMF/C_6D_6 suspension (0.5 mL, v/v' = 4/1) of 5 (5.3 mg, 0.02 mmol), iodoarenes (7; 0.10 mmol), CsF (45.6 mg, 0.30 mmol) was added α,α,α-trifluorotoluene (5.0 μL, as an internal standard). The suspension was transferred into pressure-tight NMR tube. TFE (5.0 atm, c.a. > 0.3 mmol) was then charged into the reactor. The reaction mixture was thermostated at 60 ºC for 96 h. Spectral data for compounds **8a** and **8n-r** showed good agreement with the literature data.[S4] As for these compounds **8a** and **8n–r**, we present only ^{19}F NMR data in this section.

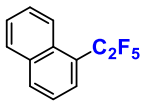


4-pentafluoroethylbiphenyl (8b): By following the general procedure ***A***, the reaction with 4-iodobiphenyl (280.5 mg, 1.00 mmol) was conducted for 65 h, yielding **8b** (263.0 mg, 0.97 mmol) as white solid. **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 7.45 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 2H), 7.65 (d, *J* = 7.4 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 8.2 Hz, 2H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 113.6 (tq, *J* = 253.3 Hz, *J* = 38.2 Hz), 119.2 (qt, *J* = 285.4 Hz, *J* = 39.5 Hz), 126.9 (t, *J* = 6.2 Hz), 127.3, 127.4, 127.5 (t, *J* = 24.1 Hz), 128.2, 129.0, 139.7, 144.8 (t, *J* = 1.5 Hz). **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –87.9 (s, 3F), –117.8 (s, 2F).

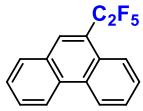


2-pentafluoroethylbiphenyl (8c): By following the general procedure ***A***, the reaction with 2-iodobiphenyl (281.3 mg, 1.00 mmol) was conducted, yielding **8c** (193.6 mg, 0.71 mmol) as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 7.29–7.33 (m, 3H), 7.39–7.41 (m, 3H), 7.53 (d, *J* = 7.3 Hz, 1H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H). **^{13}C{^{1}H} NMR (100**

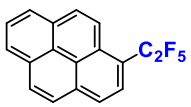
MHz, $CDCl_3$, rt, δ/ppm): 114.2 (tq, *J* = 256.3 Hz, *J* = 38.4 Hz), 119.1 (qt, *J* = 286.6 Hz, *J* = 39.3 Hz,), 126.2 (t, *J* = 21.9 Hz), 127.2, 127.3, 127.5, 127.9 (t, *J* = 7.6 Hz), 129.0, 131.1, 132.7, 140.4, 142.6 (t, *J* = 2.6 Hz). **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –86.8 (s, 3F,), –109.7 (s, 2F).



1-(perfluoroethyl)naphthalene (8d): By following the general procedure ***A***, the reaction with 1-iodonaphthalene (259.3 mg, 1.00 mmol) was conducted for 72 h, yielding **8d** (186.0 mg, 0.76 mmol) as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 7.53-7.63 (m, 3H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.93 (d, *J* = 7.6 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 8.26 (d, *J* = 8.8 Hz, 1H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 115.3 (tq, *J* = 253.1 Hz, *J* = 38.8 Hz), 119.7 (qt, *J* = 285.3 Hz, *J* = 39.3 Hz), 124.3 (br, two resonances may be overlapped), 124.7 (br), 126.4, 127.4 (t, *J* = 9.3 Hz), 127.6, 129.0, 129.9, 133.3, 134.1. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –86.1 (s, 3F), –110.9 (s, 2F).

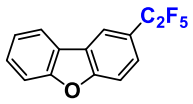


9-(pentafluoroethyl)phenanthrene (8e): By following the general procedure ***A***, the reaction with 9-iodophenanthrene (305.0 mg, 1.00 mmol) was conducted, yielding **8e** (262.8 mg, 0.89 mmol) as yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 7.60-7.80 (m, 4H), 7.96 (d, *J* = 7.8 Hz, 1H), 8.18 (s, 1H), 8.33 (d, *J* = 8.1 Hz, 1H), 8.69 (d, *J* = 8.4 Hz, 1H), 8.76 (d, *J* = 8.6 Hz, 1H). **^{13}C{1H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 115.2 (tq, *J* = 254.5 Hz, *J* = 39.1 Hz), 119.6 (qt, *J* = 287.1 Hz, *J* = 38.9 Hz), 122.6, 122.9 (t, *J* = 21.6 Hz), 123.2, 125.7 (m), 127.1, 127.3, 127.5, 129.1, 129.4, 129.9, 130.0 (t, 3*J* = 9.2 Hz), 131.0, 131.8. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –85.9 (s, 3F), –111.2 (s, 2F). **HRMS (EI)**: *m/z* Calcd for $C_{16}H_9F_5$, 296.0624, (M+) Found: 296.0627.

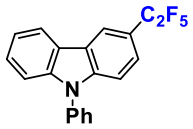


1-pentafluoroethylpyrene (8f): By following the general procedure ***A***, the reaction with 9-

iodopyrene (329.2 mg, 1.00 mmol) was conducted. Further purification was carried out by using a recycle HPLC, yielding **8f** (219.7 mg, 0.69 mmol) as pale yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 7.92 (d, *J* = 8.9 Hz, 1H), 7.95-8.07 (m, 2H), 8.08-8.20 (m, 4H), 8.23 (d, *J* = 8.2 Hz, 1H), 8.46 (d, *J* = 8.8 Hz, 1H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 113.8 (tq, *J* = 253.8 Hz, *J* = 38.2 Hz), 119.2 (qt, *J* = 285.9 Hz, *J* = 39.7 Hz), 120.5 (t, *J* = 21.8 Hz), 123.3 (m), 123.9, 124.1, 124.8, 125.2 (t, *J* = 9.4 Hz), 126.1, 126.3, 126.4, 126.8, 129.2, 129.4, 129.9, 130.8, 133.9. A ^{13}C resonance may be obscured by other aromatic resonances. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –86.4 (s, 3F), –109.9 (s, 2F). **HRMS (EI)**: *m/z* Calcd for $C_{18}H_9F_5$, 302.0624, (M+) Found: 302.0627.

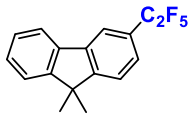


2-(pentafluoroethyl)dibenzofuran (8g): By following the general procedure ***A***, the reaction with 2-iododibenzofuran (294.2 mg, 1.00 mmol) was conducted, yielding **8g** (268.7 mg, 0.94 mmol) as white solid. **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 7.39 (tt, *J* = 7.7, 1.3 Hz, 1H), 7.52 (tt, *J* = 7.7, 0.9 Hz, 1H), 7.53–7.65 (m, 2H), 7.69 (dd, *J* = 8.6, 1.1 Hz, 1H), 7.91–7.99 (m, 1H), 8.19 (s, 1H). **^{13}C{1H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 111.9, 112.0, 113.9 (tq, *J* = 253.8 Hz, *J* = 38.2 Hz), 119.3 (qt, *J* = 286.5 Hz, *J* = 39.7 Hz), 119.5 (t, *J* = 6.7 Hz), 120.9, 123.2, 123.2 (t, *J* = 24.2 Hz), 123.3, 124.7, 125.2 (t, *J* = 6.2 Hz), 128.2, 156.8, 157.8. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –87.9 (s, 3F), –116.2 (s, 2F). **HRMS (EI)**: *m/z* Calcd for $C_{14}H_7F_5O$, 286.0417, (M+) Found: 286.0419.

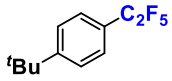


N*-phenyl-3-pentafluoroethyl-carbazole (8h)**: By following the general procedure ***A, the reaction with *N*-phenyl-3-iodo-carbazole (369.2 mg, 1.00 mmol) was conducted for 72 h, yielding **8h** (332.0 mg, 0.92 mmol) as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 7.38 (t, *J* = 7.3 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.48-7.60 (m, 5H), 7.64-7.74 (m, 3H), 8.23 (d, *J* = 7.8 Hz, 1H), 8.45 (s, 1H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 110.0 (s), 110.3 (s), 114.4 (tq, *J* = 252.0 Hz, *J* = 37.8 Hz), 119.2 (t, *J* = 6.6 Hz), 119.5 (tq, *J* = 40.5 Hz, *J* = 284.2 Hz), 120.0 (t,

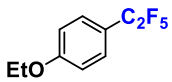
J = 24.1 Hz), 120.6, 120.8, 122.8, 123.3, 123.8 (t, J = 6.0 Hz), 127.0, 127.2, 128.2, 130.1, 137.0, 141.7, 142.6. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –87.8 (s, 3F), –115.6 (s, 2F).



2-pentafluoroethyl-9,9-dimethyl-fluorene (8i): By following the general procedure ***A***, the reaction with 2-iodo-9,9-dimethyl-fluorene (320.9 mg, 1.00 mmol) was conducted, yielding **8i** (289.0 mg, 0.93 mmol) as white solid. **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 1.59 (s, 6H), 7.42–7.50 (m, 2H), 7.52–7.60 (m, 1H), 7.69 (d, J = 7.9 Hz, 1H), 7.78 (s, 1H), 7.83–7.91 (m, 2H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 26.8, 47.1, 114.0 (tq, J = 253.8 Hz, J = 38.1 Hz), 119.4 (qt, J = 285.9 Hz, J = 40.0 Hz), 120.1, 120.8, 122.8, 125.6 (t, J = 6.4 Hz), 127.2 (t, J = 23.7 Hz), 127.3, 128.6, 137.7, 143.0, 154.0, 154.2. A ^{13}C resonance may be obscured by other aromatic resonances. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –87.8 (s, 3F), –116.8 (s, 2F). **HRMS (EI)**: *m/z* Calcd for $C_{17}H_{13}F_5$, 312.0937, (M+) Found: 312.0940.

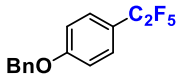


p-tert*-butyl-(pentafluoroethyl)benzene (8k)**: By following the general procedure ***A, the reaction with *p-tert*-butyl-ioodbenzene (256.2 mg, 1.00 mmol) was conducted, yielding **8k** (118.3 mg, 0.47 mmol) as pale yellow oil. It should be noted that, in the crude product, the yield of **4k** was estimated to be 81% (by ^{19}F NMR analysis using *α*,*α*,*α*-trifluorotoluene as an internal standard). **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 1.36 (s, 9H), 7.50–7.58 (AB quartet, J = 9.8 Hz, 4H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 31.1, 34.9, 113.6 (tq, J = 252.6 Hz, J = 38.1 Hz), 119.2 (qt, J = 285.7 Hz, J = 39.8 Hz), 125.7, 125.8 (t, J = 24.1 Hz), 126.2 (t, J = 6.3 Hz), 155.3. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –88.0 (s, 3F), –117.7 (s, 2F). **HRMS (EI)**: *m/z* Calcd for $C_{12}H_{13}F_5$, 252.0937, (M+) Found: 252.0941.

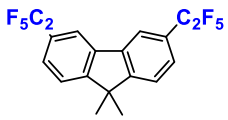


p*-ethoxy-(pentafluoroethyl)benzene (8l)**: By following the general procedure ***A, the reaction with *p*-ethoxy-ioodbenzene (248.0 mg, 1.00 mmol) was conducted, yielding **8m** (57.6 mg, 0.24

mmol) as pale yellow liquid. It should be noted that, in the crude product, the yield of **8m** was estimated to be 86% (by 19F NMR analysis using *α*,*α*,*α*-trifluorotoluene as an internal standard). **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 1.44 (t, *J* = 6.9 Hz, 3H), 4.08 (q, *J* = 6.9 Hz, 2H), 6.97 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 14.6, 63.7, 113.7 (tq, *J* = 252.7 Hz, *J* = 38.1 Hz), 114.5, 119.3 (qt, *J* = 285.8 Hz, *J* = 40.4 Hz), 120.5 (t, *J* = 24.7 Hz), 128.0 (t, *J* = 6.3 Hz), 161.7. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –88.2 (s, 3F), –117.0 (s, 2F). **HRMS (EI)**: *m/z* Calcd for $C_{12}H_{13}F_5$, 240.0574, (M+) Found: 240.0578.

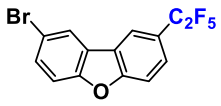


p*-benzyloxy-(pentafluoroethyl)benzene (8m)**: By following the general procedure ***A, the reaction with *p*-benzyloxy-ioodbenzene (310.1 mg, 1.00 mmol) was conducted, yielding **8l** (264.7 mg, 0.88 mmol) as pale yellow solid. It should be noted that, in the crude product, the yield of **8l** was estimated to be 90% (by ^{19}F NMR analysis using *α*,*α*,*α*-trifluorotoluene as an internal standard). **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 5.14 (s, 2H), 7.09 (d, *J* = 8.6 Hz, 2H), 7.35–7.50 (m, 5H), 7.56 (d, *J* = 8.6 Hz, 2H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 70.1, 113.6 (tq, *J* = 253.1 Hz, *J* = 38.2 Hz), 114.9, 119.2 (qt, *J* = 285.6 Hz, *J* = 40.1 Hz), 120.9 (t, *J* = 24.9 Hz), 127.5, 128.1 (t, *J* = 6.3 Hz), 128.3, 128.7, 136.2, 161.4. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –88.1 (s, 3F), –117.0 (s, 2F). **HRMS (EI)**: *m/z* Calcd for $C_{15}H_{11}F_5O$, 302.0730, (M+) Found: 302.0729.

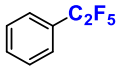


2,7-bis(pentafluoroethyl)-9,9-dimethyl-fluorene (8s): A DMF suspension (5.0 mL) of **5** (105 mg, 0.40 mmol), 2,7-diiodo-9,9-dimethyl-fluorene (**7s**; 310.1 mg, 1.00 mmol), CsF (456 mg, 3.00 mmol) was transferred into a 50 mL glass autoclave reactor. TFE (3.0 atm, *c.a.* > 6.0 mmol) was then charged into the reactor. The reaction mixture was thermostated at 80 ^{o}C for 96 h *without stirring*. After any excess of TFE was purged from the reactor (*caution*: The reaction mixture must be handled in well ventilated fume hood!!), the reaction mixture was quenched with deionized water (40 mL). Aqueous phase was extracted with Et_2O (40 mL × 5). Combined organic phase was further washed with water (40 mL × 3), and then dried over Na_2SO_4. All volatiles were

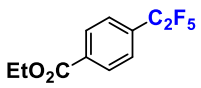
removed under reduced pressure, and the crude product was purified by silica gel column chromatography. Further purification using a recycle HPLC gave the title compound (284.2 mg, 0.66 mmol) as pale yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 1.54 (s, 6H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.71 (s, 2H), 7.87 (d, *J* = 8.0 Hz, 2H). **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 26.6, 47.5, 113.8 (tq, *J* = 253.8 Hz, *J* = 38.2 Hz), 119.2 (qt, *J* = 285.9 Hz, *J* = 39.7 Hz), 120.9, 121.0 (t, *J* = 6.3 Hz), 125.9 (t, *J* = 6.3 Hz), 128.6 (t, *J* = 23.7 Hz), 141.3, 154.6. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –88.0 (s, 6F), –117.3 (s, 4F). **HRMS (EI)**: *m/z* Calcd for $C_{19}H_{12}F_{10}$, 430.0779, (M+) Found:430.0781.



2-bromo-8-(pentafluoroethyl)dibenzofuran (8t): By following the general procedure ***A***, the reaction with 2-bromo-8-iododibenzofuran (372.8 mg, 1.00 mmol) was conducted, yielding a mixture of **8t** (285 mg, 0.78 mmol) and as white solid. **^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm)**: 7.24–7.61 (m, 4H), 7.86 (s, 1H), 7.95 (s, 1H). **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 112.2, 113.3, 113.7 (tq, *J* = 252.6 Hz, *J* = 38.0 Hz), 116.3, 119.2 (qt, *J* = 284.2 Hz, *J* = 39.7 Hz), 119.6 (t, *J* = 6.7 Hz), 123.5, 123.6 (t, *J* = 24.3 Hz), 123.7, 125.0, 125.9 (t, *J* = 6.2 Hz), 131.0, 155.3, 158.0. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –87.4 (s, 3F), –115.9 (s, 2F). **HRMS (EI)**: *m/z* Calcd for $C_{14}H_6BrF_5O$, 363.9522, (M+) Found: 363.9529.

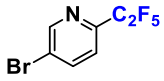


pentafluoroethylbenzene (8a): By following the general procedure ***B***, the reaction with iodobenzene (19.9 mg, 0.10 mmol) was conducted. 19F NMR analysis revealed that the title compound **8a** was obtained in >99% yield. **^{19}F NMR (376 MHz, DMF/C6D6, rt, δ /ppm)**: –88.1 (s, 3F), –117.8 (br s, 2F).

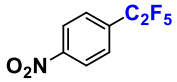


ethyl *p*-(pentafluoroethyl)benzoate (8n): By following the general procedure ***B***, the reaction with ethyl *p*-iodobenzoate (26.8 mg, 0.10 mmol) was conducted. 19F NMR analysis revealed that the title compound **8n** was obtained in 51% yield. **^{19}F NMR (376 MHz, DMF/C_6D_6, rt, δ**

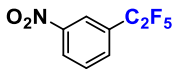
/ppm): –88.2 (s, 3F), –118.4 (br s, 2F)



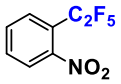
5-bromo-2-(perfluoroethyl)pyridine (8o): By following the general procedure ***A***, the reaction with *p*-benzyloxy-ioodbenzene (283.9 mg, 1.00 mmol) was conducted. 19F NMR analysis of the crude product revealed that the title compound **8o** was obtained in 30% yield. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –86.3 (s, 3F), –120.0 (s, 2F).



p*-nitro-(pentafluoroethyl)benzene (8p)**: By following the general procedure ***A, the reaction with *p*-iodo-nitrobenzene (249.0 mg, 1.00 mmol) was conducted. 19F NMR analysis of the crude product revealed that the title compound **8p** was obtained in 33% yield. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –87.7 (s, 3F), –118.0 (s, 2F).



m*-nitro-(pentafluoroethyl)benzene (8q)**: By following the general procedure ***A, the reaction with *m*-iodo-nitrobenzene (248.7 mg, 1.00 mmol) was conducted. 19F NMR analysis of the crude product revealed that the title compound **8q** was obtained in 11% yield. **^{19}F NMR (376 MHz, CDCl3, rt, δ/ppm)**: –85.0 (s, 3F), –115.0 (s, 2F).



o*-nitro-(pentafluoroethyl)benzene (8r)**: By following the general procedure ***A, the reaction with *o*-iodo-nitrobenzene (251.0 mg, 1.00 mmol) was conducted. 19F NMR analysis of the crude product revealed that the title compound **8r** was obtained in 18% yield. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –86.3 (s, 3F), –112.7 (s, 2F).

pentafluoroethylation of 1-allyloxy-2-iodobenzene (8u):

To a DMF/C_6D_6 suspension (0.5 mL, v/v' = 4/1) of 1 (5.2 mg, 0.02 mmol), 1-allyloxy-2-iodobenzene (**7u**; 16.5 μL, 0.10 mmol), CsF (45.6 mg, 0.30 mmol) was added α,α,α-trifluorotoluene (5.0 μL, as an internal standard). The suspension was transferred into a pressure-tight NMR tube (Wilmad-LabGlass 524-PV-7; total volume: 2.0 mL). TFE (5.0 atm, c.a. > 0.3

mmol) was then charged into the reactor, and the reaction mixture was heated at 80 °C for 96 h. ^{19}F NMR analysis of the crude product revealed that the conversion of 3v was 41% and that the pentafluoroethylated compound **8u** was obtained in 41% yield. It should be noted that 3-methyl-2,3-dihydrobenzofuran, which should be generated if the pentafluoroethylation proceeds via an aryl radical intermediate, was not detected by GC/MS analysis of the crude product. After any excess of TFE was purged from the reactor, the reaction mixture was quenched with deionized water (10 mL). Aqueous phase was extracted with Et_2O (10 mL × 3), and the combined Et_2O extraction was then dried over anhydrous Na_2SO_4. All volatiles were removed under reduced pressure, and the crude product was purified by silica gel column chromatography (eluate: hexane), affording **8u** (7.9 mg, 31%) as colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.60 (dm, *J* = 7.9 Hz, 2H,), 5.29 (ddt, *J* = 10.7, 1.5, 1.5 Hz, 1H,), 5.44 (ddt, *J* = 17.3, 1.5, 1.5 Hz, 1H,), 6.02 (ddm, *J* = 17.3, 10.7 Hz, 1H,), 7.00 (d, J = 8.5 Hz, 1H), 7.04 (ddm, *J* = 7.7 Hz, 1H), 7.49 (ddm, *J* = 7.9 Hz, 1H), 7.53 (dd, J = 8.0, 1.5 Hz, 1H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm)**: 69.3, 113.5, 113.7 (tq, *J* = 254.4 Hz, *J* = 38.4 Hz,), 116.9 (t, *J* = 22.5 Hz), 117.4, 119.4 (qt, *J* = 285.8 Hz, *J* = 39.6 Hz), 120.5, 128.9 (t, *J* = 8.6 Hz), 132.3, 133.3, 157.2. **^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm)**: –86.9 (s, 3F), –114.9 (s, 2F).

Monitoring of the reaction of (phen)CuI with excess amount of CsF (3.7):

Reaction was conducted in a 20 mL glass test tube equipped with a screw-cap. A DMF suspension (5.0 mL) of (phen)CuI (7.4 mg, 0.02 mmol) and CsF (45.6 mg, 0.30 mmol) was transferred into the test tube. The reaction mixture was thermostated at 80 ºC for a given time (0 and 180 min). After heating, the reaction mixture was passed through a hydrophilic-PTFE membrane filter in order to remove any insoluble residue. The resultant filtrate was further diluted with fresh DMF (5.0 mL), and a portion of the solution was then analyzed by UV-vis spectroscopy. The authentic DMF solution of **5** was prepared as follows: A DMF solution (10.0 mL) of (phen)CuF (**5**; 5.3 mg, 0.02 mmol) was passed through a hydrophilic-PTFE membrane filter, and a portion of the solution was then analyzed by UV-vis spectroscopy.

2.9. References of experimental section

S1. C. M. Wyss, B. K. Tate, J. Bacsa, M. Wieliczko, J. P. Sadighi, *Polyhedron* **2014**, *84*, 87.

S2. F. Hu, X. Lei, *ChemCatChem* **2015**, *7*, 1539.

S3. D. Zhu, J. Ma, K. Luo, H. Fu, L. Zhang, S. Zhu, *Angew. Chem. Int. Ed.* **2016**, *55*, 8452.

S4. L. Li, C. Ni, Q. Xie, M. Hu, F. Wang, J. Hu, *Angew. Chem. Int. Ed.* **2017**, *56*, 9971.

Chapter 4

CsF-catalyzed Pentafluoroethylation of Acyl Fluorides via Fluoroacylation of Tetrafluoroethylene

4.1 Introduction

The pentafluoroethyl carbonyl ($–COC_2F_5$) moiety has recently been recognized as an effective functional group for the use in pharmaceuticals and other bioactive compounds.[1] For example, a pentafluoroethyl ketone that contains a 2,4-dihydroxy-5-methyl phenyl moiety exhibits anti-infective activity (Figure 4.1),[2] while a guaiazulene that bears a pentafluoroethyl ketone moiety shows antitumor activity.[3] Moreover, a tripeptide with a pentafluoroethyl ketone moiety shows a high level of inhibition for human neutrophil elastase compared to the corresponding tripeptide bearing a trifluoromethyl ketone structure (Figure 4.1).[4]

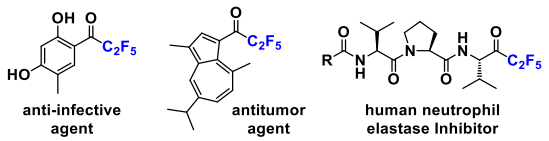


Figure 4.1. Representative bioactive pentafluoroethyl ketones

Given the utility of pentafluoroethyl ketones, several stoichiometric methods for their synthesis have been developed (Figure 4.2).[5,6] However, these reactions usually require highly reactive organometallic reagents or extremely low temperatures in order to prevent the organometallic reagents from decomposing or overreacting. Although the pentafluoroethylation of acyl chlorides with a stoichiometric amount of a pentafluoroethyl copper(I) reagent has recently been reported by Grushin and co-workers,[7] catalytic reactions for the synthesis of aromatic pentafluoroethyl ketones remain elusive.

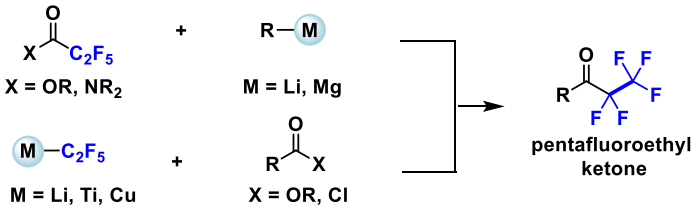
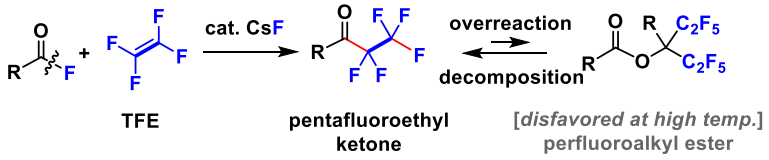


Figure 4.2. Previous work: stoichiometric synthesis of pentafluoroethyl ketones

For the generation of pentafluoroethyl matal species (M–C_2F_5), pentafluoroethyl iodide was often used, which is synthesized from TFE as shown in Chapter 1.[6] Therefore. the direct use of TFE for fluoroalkylation reactions can potentially reduce the reaction steps required and the quantity of chemical waste produced. Several organic reactions that involve the transformations of TFE into a variety of organofluorine compounds have been reported.[8,9] Furthermore, as mentioned in Chapter 2, our group has previously reported the copper(I)-catalyzed pentafluoroethylation of aryl iodides using TFE.[10] Herein, we report a cesium fluoride (CsF)-catalyzed fluoroacylation of TFE using aromatic acyl fluorides to furnish pentafluoroethyl ketones. This reaction is highly atom-economical because the amount of chemical waste produced by the reaction is less than stoichiometric. Experimental and computational studies revealed that at low temperature the reaction is in equilibrium between the pentafluoroethyl ketone and an ester bearing two pentafluoroethyl units. Furthermore, these studies suggest that a sufficiently high reaction temperature would furnish the thermodynamically favored ketone as the main product (Scheme 4.1).

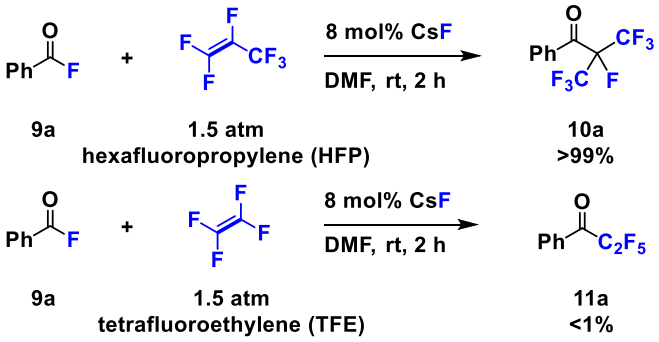


Scheme 4.1. CsF-catalyzed pentafluoroethylation of acyl fluorides

4.2 Perfluoroalkylation of benzoyl fluoride with HFP and TFE

In 1982, Knunyants reported an example of the perfluoroisopropylation of benzoyl fluoride (**9a**) by bubbling hexafluoropropylene (HFP) through the reaction mixture in the presence of a

catalytic amount of CsF.[11] The reaction conditions employed in that study were used as the basis to examine the fluoroacylation of HFP here (Scheme 4.2a). The reaction of acyl fluoride **9a** at room temperature under HFP atmosphere (1.5 atm) furnished the corresponding ketone **10a** in quantitative yield (>99%). On the other hand, only a trace amount of the desired pentafluoroethyl ketone **11a** was obtained when TFE was employed under otherwise identical reaction conditions (Scheme 4.2b: <1%). These results indicate that HFP reacts more readily with CsF than TFE to give the corresponding fluoroalkyl anion.



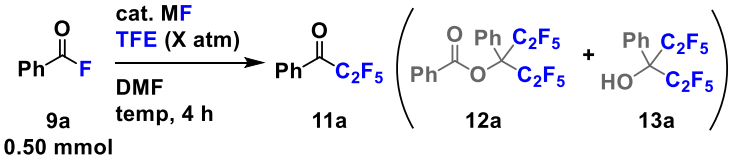
Scheme 4.2. Perfluoroalkylation of benzoyl fluoride using perfluoroalkene and CsF

4.3 Optimization of reaction conditions

To obtain the desired pentafluoroethyl ketone, we optimized the reaction conditions for the fluoroacylation of TFE with acyl fluoride **9a** (Table 4.1). A pressure-tight tube (total volume: 12 mL) was used as the reaction vessel for the screenings (Table 1). At high temperature (120 °C) and high TFE pressure (5.0 atm; >4.0 equiv. of TFE) **11a** was obtained in moderate yield (entry 1: 55%) with several side products according to the ^{19}F NMR spectrum. A major side product was assigned to an ester bearing two pentafluoroethyl groups (**12a**). A tertiary alcohol (**13a**) was also identified as a minor side product. Furthermore, monitoring the mixture during the course of the reaction indicated that, after 1 hour, the ester **12a** was present in almost the same amount as ketone **11a** (entry 2: **12a**: 34%; **11a**: 31%). However, only a trace amount of ester **12a** remained after an additional 3 hours (entry 2: 3%) and the yield of ketone **11a** had increased. This observation indicated that ester **12a** was likely to be an intermediate in this reaction. A lower TFE pressure improved the yield of the desired product (entry 2: 2.5 atm; **11a**: 71%, **12a**: 2%). When the catalyst loading was lowered (5 mol%), the yield of **11a** decreased

slightly and the yield of **12a** increased (entry 4; 2a: 65%, **12a**: 11%). Upon further lowering the TFE pressure (1.5 atm), the yield of 11a also further improved (entry 5; **11a**: 74%, **12a**: 3%). Increasing the reaction temperature (140 °C) also increased the reaction efficiency (entry 6; **11a**: 82%, **12a**: 0%). Subsequently, various alkali metal fluorides were tested; we found that reactions with LiF or NaF showed no conversion of acyl fluoride **9a** (entries 7, 8), while the reaction with KF furnished **12a** in low yield (entry 9; **11a**: 25%, **12a**: 3%). The results indicated that the more ionic radius of the alkali metal fluorides as catalysts is larger, the reactivity is higher. The alkali earth metal fluoride CaF_2 did not work for this reaction system (entry 10). Accordingly, we concluded that the reaction conditions listed in entry 5 are the most suitable for this fluoroacylation reaction.

Table 4.1. Optimization of reaction conditions



entry	MF	mol%	X / atm	Temp. / °C	Yield of 12a / %[a]	Yield of 13a / %[b]
1	CsF	10	5.0	120	55 (31)[c]	3 (34)[c]
2	CsF	10	2.5	120	71	2
3	CsF	5	2.5	120	65	11
4	CsF	5	1.5	120	74	3
5	CsF	5	1.5	140	82	0
6	LiF	5	1.5	140	0	0
7	NaF	5	1.5	140	0	0
8	KF	5	1.5	140	25	3
9	CaF_2	5	1.5	140	0	0

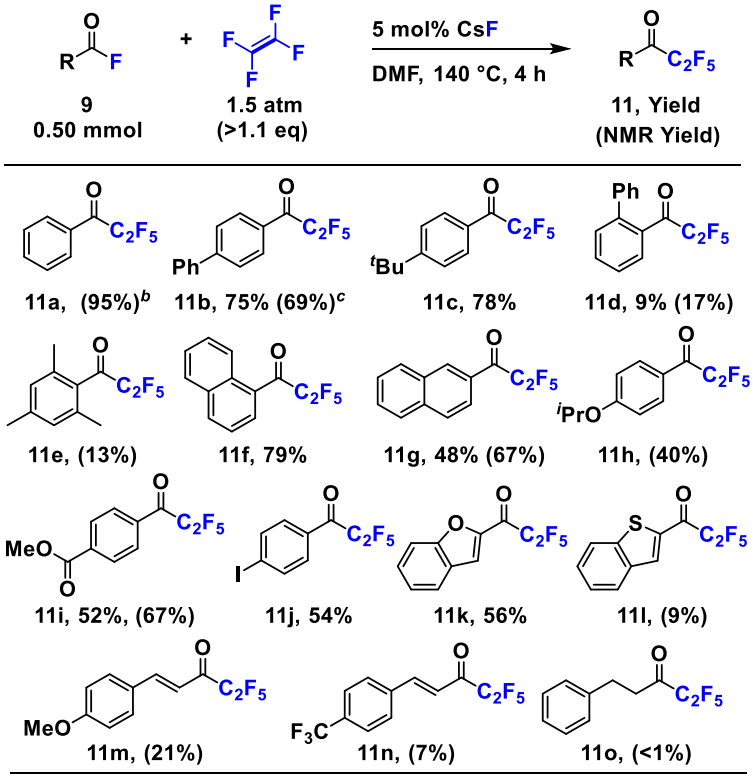
[a]Yields were determined by ^{19}F NMR using $PhCF_3$ as an internal standard. [b]The yield of ester 12a was estimated based on the consumption of two molecules of acyl fluoride 9a. [c] The reaction was conducted for 1 h.

4.5 Substrate scope

With the optimized reaction conditions in hand, the ‡luoroacylation of TFE was carried out using different aromatic acyl fluorides (Table 2). The reaction using benzoyl fluoride **9a** furnishes ketone **11a** in excellent yield (95%). The reactions using acyl fluorides **9b** and **9c**, which bear phenyl or *tert*-butyl groups at the para-position,

respectively, showed high reactivity (**11b**: 75%; **11c**: 78%). The gram-scale synthesis of the ketone **11b** was also applicable (**11b**: 69%, 1.25 g). However, sterically hindered acyl fluorides **9d** and **9e**, which bear substituents at the *ortho*-positions, showed lower reactivity under these conditions [**11d**: 9% (17%); **11e**: (13%)]. The CsF-catalyzed ‡luoroacylation using substrates **9f** and **9g**, which bear a naphthalene moiety, furnished the pentafluoroethyl ketones **11f** and **11g** in high to moderate yield [**11f**: 79%; **11g**: 48% (67%)]. The CsF-catalyzed ‡luoroacylation of TFE using acyl fluorides showed also good functional-group tolerance. Pentafluoroethyl ketones **11h**, **11i**, and **11j**, which bear an ether, ester, or iodide moiety, respectively, were obtained in moderate yield [**11h**: (40%); **11i**: 52% (67%); **11j**: 54%]. In the case of the reaction of an acyl fluoride bearing an iodine atom (**9j**), the aryl iodide moiety remained intact after the reaction. This result stands in contrast to the results obtained by Grushin, where both the acyl chloride and aryl iodide moieties reacted with the pentafluoroethyl copper(I) nucleophile.[7] Benzofuran derivative **9k** furnished ketone **11k** in good yield (56%), while acyl fluoride **9l**, which bears a benzothiophene moiety, generated **11l** in low yield [(9%)]. The reactions using the α,β-conjugated acyl fluorides **9m** and **9n** proceeded, albeit that the yields of the ketones were low [**11m**: (21%); **11n**: (7%)]. The alkyl acyl fluoride **9o** did not react under the reaction conditions [**11o**: (<1%)].

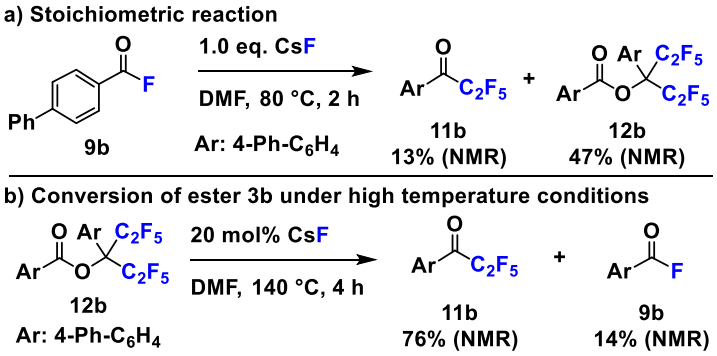
Table 4.2. Substrate scope



[a]NMR yields were determined by ^{19}F NMR spectroscopy using $PhCF_3$ as an internal standard. [b]Reaction was conducted on the 1.0 mmol scale. [c]Reaction was conducted on the 6.0 mmol scale.

4.5 Stoichiometric Reactions

To elucidate the reaction mechanism for this CsF-catalyzed fluoroacylation of TFE with acyl fluorides, a mechanistic study was conducted (Scheme 4.3). The stoichiometric reaction of biphenyl-4-carboxylic acid fluoride (**9b**) with CsF at 80 °C for 2 hours afforded ester **12b** as the major product (47%) and the corresponding ketone **11b** in low yield (13%) (Scheme 4.3a). Subsequently, ester **12b**, obtained from the stoichiometric reaction, was subjected to the optimized reaction conditions (Scheme 4.3b). When a DMF solution of ester **12b** was treated at high temperature (140 °C) with a catalytic amount of CsF, **12b** was fully consumed to give the ketone **11b** in high yield (**11b**: 76%). However, acyl fluoride **9b** was also obtained in a lower yield than ketone **11b** (**9b**: 14%). The result suggests that ester **12b**, generated from the acyl fluoride (e.g. Table 4.1, Entry 1), can be decomposed by the CsF catalyst to give the desired product **11b** and acyl fluoride **9b**.



Scheme 4.3. Isolation and reactivity of intermediate **12b**

4.5 Computational study[12]

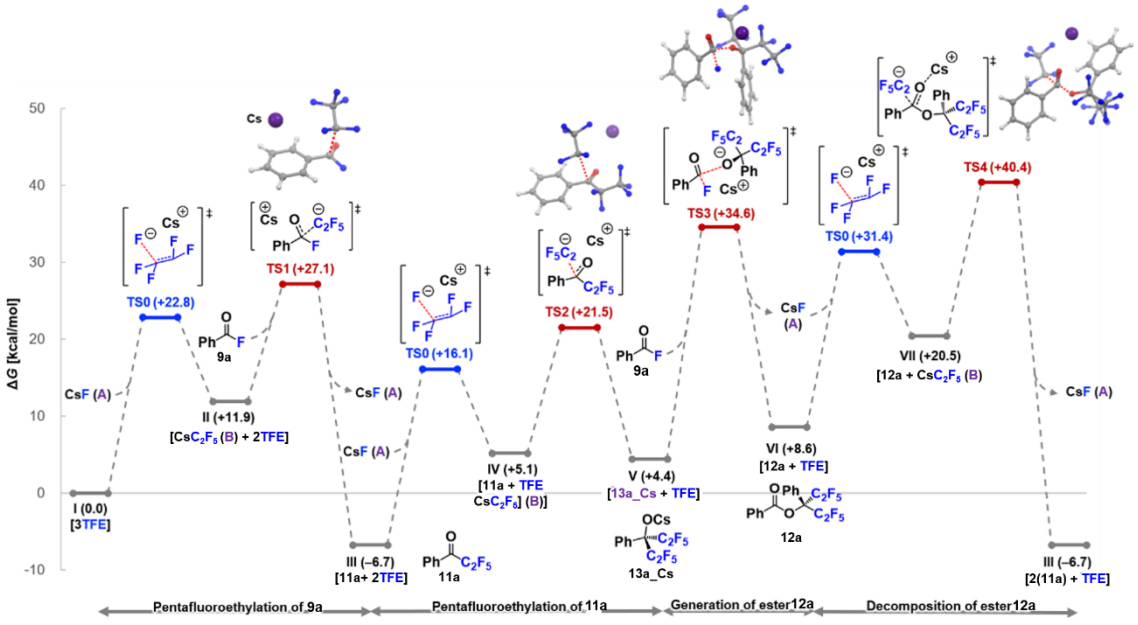
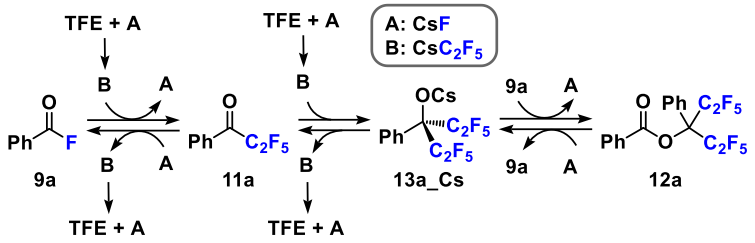


Figure 4.3. Computational study for the entire reaction pathway; all calculations were carried out at the B3LYP-D3/6-311++G(d,p), SDD for Cs/SMD(DMF,ε=37.219)//B3LYP-D3/6-31+G(d,p), LanL2DZ for Cs/SMD(DMF,ε=37.219), 413.15 K levels of theory.

In order to investigate the reaction mechanism, we carried out density functional theory (DFT) calculations (Figure 4.3). The calculations relating to the change from state I to state II, i.e., the reaction between TFE and CsF (**A**) to give pentafluoroethyl cesium

(**B**), indicated that this process should be endothermic, as **B** is significantly less stable than state I (II: ΔG = +11.9 kcal/mol). Furthermore, the estimated activation energy (**TS0**) for the formation of **B** was reasonable for a reaction that proceeds at 140 ºC (**TS0**: $\Delta G^{\ddagger}$ = +22.8 kcal/mol). The results of these calculations agree well with the experimentally observed results, i.e., that **B** was not observed in the reaction mixture. Subsequently, we calculated the activation energy for the nucleophilic addition of **B** to acyl fluoride **9a** and found it sufficiently low to proceed at 140 ºC (**TS1**: $\Delta G^{\ddagger}$ = +27.1 kcal/mol). The elimination of **A** from the resulting intermediate furnishes pentafluoroethyl ketone **11a** via an almost barrierless process. The DFT calculations also suggested that the activation energy for the pentafluoroethylation of ketone **11a** to give the cesium *tert*-alkoxide **13a_Cs** should be slightly higher than that of the nucleophilic attack on acyl fluoride **9a** [**TS2**: $\Delta G^{\ddagger}$ = +28.2 kcal/mol; **TS1**: $\Delta G^{\ddagger}$ = +27.1 kcal/mol; $\Delta\Delta G^{\ddagger}$(**TS2**–**TS1**) = +1.1 kcal/mol]. However, this extra addition step would be disfavored with respect to the thermodynamic stability of **13a_Cs** as the formation of cesium *tert*-alkoxide **13a_Cs** is an endothermic process (**V**: ΔG = +4.4 kcal/mol). Furthermore, the calculated pathway for the formation of ester **12a** revealed that the activation energy for the nucleophilic attack of **13a_Cs** onto the acyl fluoride **9a** (**TS3**) is significantly higher than that of the transition state (**TS1**) for the generation of the ketone **11a** [**TS3**: $\Delta G^{\ddagger}$ = +34.6 kcal/mol; **TS1**: $\Delta G^{\ddagger}$ = +27.1 kcal/mol; $\Delta\Delta G^{\ddagger}$(**TS3**–**TS1**) = +7.5 kcal/mol]. Moreover, the formation of the ester is thermodynamically disfavored (**VI**: ΔG = +8.6 kcal/mol), which suggests that the equilibrium between ketone **11a** and ester **12a** is extremely imbalanced and would provide ketone **11a** as the major product in the reaction mixture. This result is also in agreement with the experimental results that ester **12a** is not detected at high reaction temperatures (140 ºC; Table 4.1, entries 5 and 6) and decomposes into ketone **11** and acyl fluoride **9** under the optimized conditions (Scheme 4.3). The energetic analysis of the decomposition of ester **12a** (**TS4**), where the nucleophilic attack of **B** to ester **12a** furnishes ketone **11a** and cesium alkoxide **13a_Cs**, was also examined. The activation energy was found to be extremely high compared to other transition states (**TS1**–**3**) (**TS4**: $\Delta G^{\ddagger}$ = +40.4 kcal/mol). A series of the DFT calculations on the reaction pathway suggested that the reaction between acyl fluoride **9a** and TFE in the presence of CsF at 140 ºC should generate only pentafluoroethyl ketone **11a**.

Table 4.3. Temperature-dependent relative Gibbs free energies of **11a**, **13a_Cs**, and **12a**[a]



Temp. / [°C]	I (9a) ΔG(TΔS) (kcal/mol)	III (11a) ΔG(TΔS) (kcal/mol)	V (13a_Cs) ΔG(TΔS) (kcal/mol)	VI (12a) ΔG(TΔS) (kcal/mol)
140	0.0 (0.0)	–6.7 (–18.7)	+4.4 (–55.8)	+8.6 (–58.9)
80	0.0 (0.0)	–9.4 (–15.8)	–3.8 (–48.1)	0.0 (–50.7)
25	0.0 (0.0)	–11.6 (–13.8)	–11.3 (–40.9)	–7.9 (–43.2)

[a]All calculations were carried out at the B3LYP-D3/6-311++G(d,p), SDD for Cs/SMD(DMF, ε=37.219)//B3LYP-D3/6-31+G(d,p), LanL2DZ for Cs/SMD(DMF, ε=37.219), 413.15 K levels of theory.

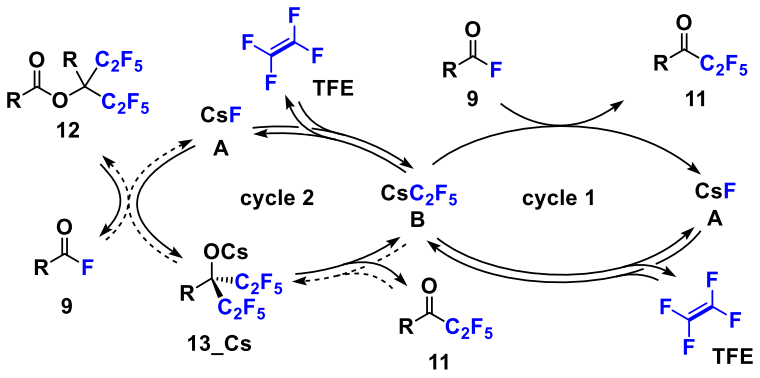
As the experimental study had suggested that the equilibrium between ketone **2** and ester **3** is affected by the reaction temperature, we investigated the temperature dependence of the product selectivity by the DFT calculation studies. Table 4.3 shows the proposed reaction pathway and the energetic analysis of the fluoroacylation at various temperatures. Although the generation of pentafluoroethyl ketone **2a** is an exothermic process at 25–140 °C, the Gibbs free energy for the formation of cesium *tert*-alkoxide **13a_Cs** strongly depends on the temperature. Notably, the formation of **13a_Cs** is disfavored at 140 °C and only becomes more favored at low temperature (< 80 °C) [140 °C: ΔG = +4.4 kcal/mol; 80 °C: ΔG = –3.8 kcal/mol; 25 °C: ΔG = –11.3 kcal/mol]. The comparison of the thermodynamic stability of ester **12a** revealed that the formation of **12a** is also favored at lower temperatures [140 °C: ΔG = +8.6 kcal/mol; 80 °C: ΔG = 0.0 kcal/mol; 25 °C: ΔG = –7.9 kcal/mol]. The results of these calculations are in good agreement with the experimental results, which the ester **12a** was detected at lower temperature (Table 4.1, entries 1–4; Scheme 1).

A detailed energetic analysis indicated that any differences in the relative free energy values are strictly controlled by the relative entropy (ΔS) of formation. The product of the relative entropy and the temperature ($T\Delta S$) is significantly higher for ketone **11a** than for

alkoxide **13a_Cs** and ester **12a** (**9a**: TΔS = –18.3 – –13.8 kcal/mol; **13a_Cs**: TΔS = –55.8 – –40.9 kcal/mol; **11a**: TΔS = –58.9 – –43.2 kcal/mol). This trend is consistent with the observation that the pentafluoroethylation of ketone **11a** by the pentafluoroethyl cesium species **B**, generated from TFE and CsF (**A**), is a process to give one product (**13a_Cs**) from three components [**11a** + CsF (**A**) + TFE]. Conversely, the pentafluoroethylation of **9a** to form **11a** can be regarded as a process to give two components [**11a** + CsF (**A**)] from three components [**9a** + CsF (**A**) + TFE]. The relative entropy change $\Delta\Delta S$ between alkoxide **13a_Cs** and ester **12a** is relatively small because the formation of ester **12a** is a process to give two components [**12a** + CsF (**A**)] from two components [**9a** + **13a_Cs**]. These results suggest that higher temperatures are essential to thermodynamically destabilize the side-product **12a**.

4.6 A possible reaction mechanism

Based on the experimental and computational studies, we would like to propose a feasible catalytic cycle for the CsF-catalyzed fluoroacylation of TFE with acyl fluorides (Scheme 4.4). The proposed catalytic reaction consists of two catalytic cycles. The first catalytic cycle is the formation of ketone **11** (cycle 1). Initially, the pentafluoroethyl cesium species B, a nucleophilic intermediate, would be generated from the reaction with CsF (**A**) and TFE. The resulting intermediate B would then react with acyl fluoride **9** to give the desired pentafluoroethyl ketone **11** and regenerate CsF (**A**). This catalytic cycle would be the main pathway for the formation of ketone **11**. The second catalytic cycle is the formation of ester **12** (cycle 2). Ketone **11** would react with **B** to give the cesium alkoxide **13_Cs** due to the high electrophilicity of ketone **11**. Furthermore, the resulting cesium alkoxide **4_Cs** would react with acyl fluoride **9** to give **A** and ester **12** as a side product. The catalytic cycle for the formation of ester **12** (cycle 2) would operate as a minor reaction pathway at low temperatures.



Scheme 4.4. A plausible reaction mechanism

4.7 Conclusion

In Chapter 4, we have developed a CsF-catalyzed fluoroacylation of TFE using aromatic acyl fluorides to furnish a series of pentafluoroethyl ketones. This reaction proceeds smoothly at low TFE pressure. The experimental results suggest that, at low temperature, an ester bearing two pentafluoroethyl groups is generated as a transient intermediate. Conducting the reaction at high temperature is essential to ensure a high reaction efficiency. Computational studies indicated that the reaction mechanism is complex and includes an equilibrium between the ketone and ester products. A simulation of the reaction at various temperatures revealed that the temperature-dependent thermodynamic stability of the products and side products is the key to providing the ketone as the main product in high yield.

4.8 References and notes

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[25] For details of DFT calculations of the energies and structures in the transition states, see the Experimental section.

4.9 Experimental section

Preparation of anhydrous Me_4N•F.

According to a following the previously reported method, under air, Me_4NF•$4H_2O$ was dried.[S1] Me_4NF•$4H_2O$ was placed in a round bottom flask. The solid was heated at 150 °C for 2 days under reduced pressure. After heating, the flask was brought into grove box. The resulting solid was recrystallized from 2-propanol. After removal of solvents, anhydrous Me_4N•F was obtained as a white powder.

Synthesis of Me_4N•SCF_3.

Me_4N•SCF_3 was synthesized by a following the previously reported method.[S2] Elemental sulfur (160 mg, 5.00 mmol) was added to a 100 mL round bottom flask followed by THF (40 mL) at room temperature. $TMSCF_3$ (0.800 mL, 5.41 mmol) was added to the mixture. Then, the reaction mixture was cooled to −60 °C. Me_4N•F (0.500 g, 5.37 mmol) was added slowly over 30 min. The reaction mixture was stirred at −60 °C for 30 min and then allowed to warm to room temperature. Additionally, the mixture was stirred for 16 hours. A precipitation was filtered off. Then, the resulting crude material was washed with diethyl ether to give the desired product Me_4N•SCF_3 as a pale orange solid in 82% yield (718 mg, 4.10 mmol). **^{1}H NMR (CD_3CN, 400 MHz)**: δ = 3.14 (s, 12H). ^{19}F NMR (CD_3CN, 376 MHz): δ = –10.8. **^{13}C NMR (CD_3CN, 100 MHz)**: δ = 56.1 (m), 145.4 (q, J_{CF} = 293.1 Hz).

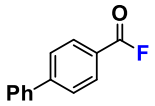
Procedures of preparation of acyl fluoride 9.

Method A[S3]: Under N_2 atmosphere, the corresponding carboxylic acid (3.00 mmol) was transferred to a PFA bottle equipped with a stirrer bar. After addition of CH_2Cl_2 (5.00 mL) to the bottle, the reaction mixture was cooled at 0 °C in ice bath. Then, Deoxo-fluor® (0.560 mL, 3.04 mmol) was added to the solution. The bottle was capped, and the reaction mixture was stirred at

0 °C for 5–30 min (written at each substrate in parentheses). The reaction was quenched by addition of aqueous $NaHCO_3$. The mixture was extracted with CH_2Cl_2 (10.0 mL) three times. The combined organic layer was dried over Na_2SO_4. Solvents were removed under reduced pressure. The crude material was purified by silica gel column chromatography (hexane/AcOEt = 97:3) to give the corresponding acid fluoride.

Method B[S4]: Under N_2 atmosphere, the corresponding carboxylic acid (1.00 mmol) was transferred to a PFA bottle equipped with a stirrer bar. To the reaction vessel, $Me_4N•SCF_3$ (230 mg, 1.31 mmol) and CH_2Cl_2 (5.00 mL) were added. Then, the reaction mixture was stirred until completely consumption of $Me_4N•SCF_3$. The resulting suspension was filtered through a silica gel pad. Solvents were removed under reduced pressure. The crude material was purified by silica gel column chromatography (hexane/AcOEt = 97:3) to give the corresponding acid fluoride.

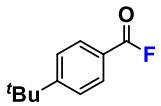
Characterization of acyl fluoride 9.



Biphenyl-4-carboxylic acid fluoride (9b): Method A (5 min) with biphenyl-4-carboxylic acid (595 mg, 3.00 mmol) gave the title compound **9b** as a white solid in 73% yield (439 mg, 2.19 mmol).

1H NMR ($CDCl_3$, 400 MHz): δ = 8.12 (d, J = 8.2 Hz, 2H), 7.75 (d, J = 8.0 Hz, 2H), 7.64 (d, J_{HH} = 7.1 Hz, 2H), 7.50 (dd, J = 7.2, 7.2 Hz, 2H), 7.44 (dd, J = 7.2, 7.2 Hz, 1H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 15.4 (s, 1F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 157.3 (d, J = 343.3 Hz), 148.0 (s), 139.2 (s), 131.9 (d, J = 3.9 Hz), 129.1 (s), 128.8 (s), 127.6 (s), 127.3 (s), 123.4 (d, J = 61.2 Hz). HRMS (EI): *m/z* $[M]^+$ calcd for $C_{13}H_9FO$: 200.0637; Found: 200.0638.

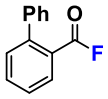
The analytical data are in agreement with those reported previously in the literature.[S5]



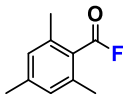
4-*tert*-Butylbenzoyl fluoride (9c): Method A (10 min) with *p-tert*-butylbenzoic acid (890 mg, 4.99 mmol) gave the title compound **9c** as a colorless oil in 70% yield (632 mg, 3.51 mmol).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.97 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 8.5 Hz, 2H), 1.36 (s, 9H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 15.0 (s, 1F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 159.5 (s)

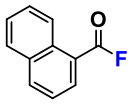
157.4 (d, J = 342.8 Hz), 131.3 (d, J = 3.9 Hz), 126.1 (s), 122.0 (d, $^{2}J_{CF}$ = 61.0 Hz), 35.4 (s), 30.9 (s). HRMS (EI): *m/z* $[M]^{+}$ calcd for $C_{11}H_{13}FO$: 180.0950; Found: 180.0953.
The analytical data are in agreement with those reported previously in the literature.[S6]



Biphenyl-2-carboxylic acid fluoride (9d): Method B with biphenyl-2-carboxylic acid (198 mg, 0.999 mmol) gave the title compound **9d** as a colorless oil in 62% yield (124 mg, 0.619 mmol).
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.05 (d, J = 7.9 Hz, 1H), 7.68 (ddd, J = 7.6, 7.6 1.3 Hz, 1H), 7.53–7.40 (m, 5H), 7.33–7.36 (m, 2H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 32.3 (s, 1F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 157.5 (d, $^{1}J_{CF}$ = 347.9 Hz), 145.5 (d, J_{CF} = 2.3 Hz), 140.1 (s), 133.9 (s), 132.1 (d, J = 2.9 Hz), 131.7 (d, J = 2.7 Hz), 128.4 (s), 128.2 (s), 127.9 (s), 127.6 (s), 124.1 (d, J = 56.9 Hz). HRMS (EI): *m/z* $[M]^{+}$ calcd for $C_{13}H_9FO$: 200.0637; Found: 200.0637.
The analytical data are in agreement with those reported previously in the literature.[S5]

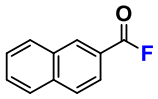


2,4,6-Trimethylbenzoyl fluoride (9e): Method A (10 min) with 2,4,6-trimethylbenzoic acid (499 mg, 3.04 mmol) gave the title compound **9e** as a white solid in 68% yield (342 mg, 2.06 mmol).
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 6.94 (s, 2H), 2.45 (d, J = 3.4 Hz, 6H), 2.32 (s, 3H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 49.6 (m, 1F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 158.5 (d, J = 352.4 Hz), 142.7 (s), 139.5 (s), 129.6 (d, J = 1.5 Hz), 123.4 (d, J_{CF} = 53.9 Hz), 21.2(s), 21.1 (d, J = 3.1 Hz). HRMS (EI): *m/z* $[M]^{+}$ calcd for $C_{10}H_{11}FO$: 166.0794; Found: 166.0796.
The analytical data are in agreement with those reported previously in the literature.[S7]

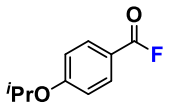


1-Naphtoic acid fluoride (9f): Method A (5 min) with 1-naphtoic acid (517 mg, 3.00 mmol) gave the title compound **9f** as a white solid in 59% yield (306 mg, 1.76 mmol).
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.01 (d, J = 8.7 Hz, 1H), 8.33 (d, J = 7.3 Hz, 1H), 8.15 (d, J =

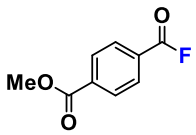
8.2 Hz, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.71 (dd, J = 7.5, 7.5 Hz, 1H), 7.60 (dd, J = 7.4, 7.4 Hz, 1H), 7.54 (dd, J = 7.8, 7.8 Hz, 1H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 27.3 (s, 1F). **$^{13}C\{^1H\}$ NMR ($CDCl_3$,100 MHz)**: δ =: 156.3 (d, J = 344.6 Hz), 136.6 (s), 133.7 (d, J = 4.0 Hz), 133.6 (d, J = 1.7 Hz), 132.0 (d, J = 7.3 Hz), 129.1 (s), 128.9 (s), 126.9 (s), 125.1 (s), 124.4 (s), 120.2 (d, J = 56.0 Hz). HRMS (EI): *m/z* $[M]^+$ calcd for $C_{11}H_7FO$: 174.0481; Found: 174.0484.
The analytical data are in agreement with those reported previously in the literature.[S8]



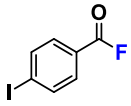
2-Naphtoic acid fluoride (9g): Method A (10 min) with 2-naphtoic acid (517 mg, 3.00 mmol) gave the title compound **9g** as a white solid in 49% yield (257 mg, 1.48 mmol).
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.65 (s, 1H), 8.02-7.92 (m, 4H), 7.69 (dd, J = 7.4, 7.4 Hz, 1H), 7.62 (dd, J = 7.4, 7.4 Hz, 1H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 15.4 (s, 1F). **$^{13}C\{^1H\}$ NMR ($CDCl_3$,100 MHz)**: δ = 157.6 (d, J = 343.6 Hz), 136.4 (s), 134.0 (d, J = 3.2 Hz), 132.3 (s), 129.7 (s), 129.6 (s), 129.1 (s), 128.0 (s), 127.4 (s), 125.6 (d, J = 4.2 Hz), 122.0 (d, J = 60.4 Hz). HRMS (EI): *m/z* $[M]^+$ calcd for $C_{11}H_7FO$: 174.0481; Found: 174.0480.
The analytical data are in agreement with those reported previously in the literature.[S6]



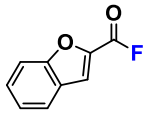
4-Isopropoxybenzoyl fluoride (9h): Method A (10 min) with 4-isopropoxybenzoic acid (547 mg, 3.04 mmol) gave the title compound **9h** as a colorless oil in 62% yield (342 mg, 1.88 mmol).
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.97 (d, J = 8.8 Hz, 2H), 6.94 (d, J = 8.0 Hz, 2H), 4.67 (sept, J = 6.1 Hz, 1H), 1.38 (d, J = 6.0 Hz, 6H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 13.0 (s, 1F). **$^{13}C\{^1H\}$ NMR ($CDCl_3$,100 MHz)**: δ = 163.8 (s), 157.2 (d, J = 339.5 Hz), 133.7 (d, J = 4.1 Hz), 116.1 (d, J = 61.7 Hz), 115.6 (s), 70.5 (s), 21.7 (s). HRMS (EI): *m/z* $[M]^+$ calcd for $C_{10}H_{11}FO_2$: 182.0743; Found: 182.0740.



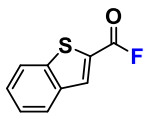
Methyl 4-(fluorocarbonyl)benzoate (9i): Method B with monomethyl terephthalate (181 mg, 1.00 mmol) gave the title compound **9i** as a white solid in 40% yield (72.5 mg, 0.398 mmol).
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.18 (d, *J* = 8.4 Hz, 2H), 8.11 (d, *J* = 8.4 Hz, 2H), 3.97 (s, 3H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 17.4 (s, 1F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 165.6 (s), 156.5 (d, *J* = 345.8 Hz), 136.0 (s), 131.4 (d, *J* = 3.7 Hz), 130.1 (s), 128.6 (d, *J* = 61.8 Hz), 52.7 (s). HRMS (EI): *m/z* $[M]^+$ calcd for $C_9H_7FO_3$: 182.0379; Found: 182.0381.
The analytical data are in agreement with those reported previously in the literature.[S9]



4-Iodobenzoyl fluoride (9j): Method A (15 min) with 4-iodobenzoic acid (744 mg, 3.00 mmol) gave the title compound **9j** as a white solid in 68% yield (513 mg, 2.05 mmol).
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.90 (dd, *J* = 8.5, 0.96 Hz, 2H), 7.73 (d, *J* = 8.4 Hz, 2H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 15.6 (s, 1F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 157.0 (d, *J* = 344.0 Hz), 138.5 (s), 132.4 (d, *J* = 3.8 Hz), 124.3 (d, *J* = 62.4 Hz), 104.0 (s). HRMS (EI): *m/z* $[M]^+$ calcd for C_7H_4FIO: 249.9291; Found: 249.9293.



Benzofuran-2-carbonyl fluoride (9k): Method B with benzofuran-2-carboxylic acid (162 mg, 0.999 mmol) gave the title compound **9k** as a yellow solid in 75% yield (123 mg, 0.749 mmol).
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.77 (s, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.62 (dd, *J* = 8.4, 0.64 Hz, 1H), 7.56 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.38 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 14.7 (s, 1F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 156.9 (d, *J* = 2.2 Hz), 149.4 (d, *J* = 329.9 Hz), 139.8 (d, *J* = 89.4 Hz), 129.5 (s), 126.3 (s), 124.6 (s), 123.5 (s), 119.3 (s), 112.6 (s). HRMS (EI): *m/z* $[M]^+$ calcd for $C_9H_5FO_2$: 164.0274; Found: 164.0272.
The analytical data are in agreement with those reported previously in the literature.[S9]

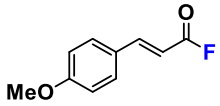


Benzo[b]thiophene-2-carbonyl fluoride (9l): Method B with benzo[b]thiophene-2-carboxylic acid (179 mg, 1.00 mmol) gave the title compound **9l** as a yellow solid in 86% yield (155 mg,

0.860 mmol).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.22 (s, 1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.91 (dd, *J* = 8.3, 0.76 Hz, 1H), 7.56 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 7.48 (ddd, *J* = 8.1, 7.1, 1.0 Hz, 1H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 21.9 (s, 1F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 153.1 (d, *J* = 335.2 Hz), 143.6 (s), 138.1 (s), 135.1 (d, *J* = 2.3 Hz), 128.4 (s), 126.7 (d, *J* = 74.8 Hz), 126.3 (s), 125.6 (s), 122.9 (s). HRMS (EI): *m/z* $[M]^+$ calcd for $C_9H_5FO_2$: 180.0045; Found: 180.0046.

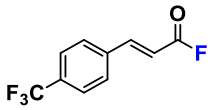
The analytical data are in agreement with those reported previously in the literature.[S10]



(*E*)-3-(4-Methoxyphenyl)acryloyl fluoride (9m): Method A (30 min) with 4-methoxycinnamic acid (535 mg, 3.00 mmol) gave the title compound **9m** as a white solid in 70% yield (381 mg, 2.11 mmol).

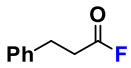
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.78 (d, *J* = 15.9 Hz, 1H), 7.51 (d, *J* = 8.6 Hz, 2H), 6.94 (d, *J* = 8.6 Hz, 2H), 6.21 (dd, *J* = 15.9, *J* = 7.3 Hz, 1H), 3.86 (s, 3H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 21.7 (s, 1F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 162.6 (s), 157.5 (d, *J* = 336.6 Hz), 151.1 (d, *J* = 6.3 Hz), 130.6 (s), 125.9 (s), 114.6 (s), 109.1 (d, *J* = 67.2 Hz), 55.4 (s). HRMS (EI): *m/z* $[M]^+$ calcd for $C_{10}H_9FO_2$: 180.0587; Found: 180.0587.

The analytical data are in agreement with those reported previously in the literature.[S11]



(*E*)-3-(4-Trifluoromethylphenyl)acryloyl fluoride (9n): Method A (30 min) with 4-trifluoromethylcinnamic acid (649 mg, 3.00 mmol) gave the title compound **9n** as a white solid in 42% yield (273 mg, 1.25 mmol).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.85 (d, *J* = 16.0 Hz, 1H), 7.71 (d, *J* = 8.6 Hz, 2H), 7.68 (d, *J* = 8.6 Hz, 2H), 6.46 (dd, *J* = 16.0 Hz, *J* = 7.0 Hz, 1H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 24.8 (d, *J* = 6.7 Hz, 1F), –65.0 (s). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 156.4 (d, *J* = 339.7 Hz), 149.3 (d, *J* = 5.9 Hz), 136.3 (s), 133.1 (q, *J* = 32.9 Hz), 128.8 (s), 126.1 (q, *J* = 3.8 Hz), 123.6 (q, *J* = 272.4 Hz), 114.8 (d, *J* = 68.1 Hz). HRMS (EI): *m/z* $[M]^+$ calcd for $C_{10}H_6F_4O$: 218.0355; Found: 218.0357.



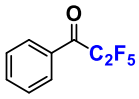
3-Phenylpropanoic acid fluoride (9o): Method A (10 min) with 3-phenylpropanoic acid (451 mg, 3.00 mmol) gave the title compound **9o** as a colorless oil in 32% yield (144 mg, 0.946 mmol). **^{1}H NMR ($CDCl_3$, 400 MHz)**: 7.33 (d, J = 7.3 Hz, 2H), 7.27–7.21 (m, 3H), 3.01 (t, J = 7.6 Hz, 2H), 2.84 (t, J = 7.6 Hz, 2H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = 42.6 (s, 1F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: 162.8 (d, J = 360.4 Hz), 138.9 (s), 128.7 (s), 128.2 (s), 126.8 (s), 33.8 (d, J = 50.4 Hz), 29.9 (d, J = 2.2 Hz). HRMS (EI): *m/z* $[M]^+$ calcd for C_9H_9FO: 152.0637; Found: 152.0636.

The analytical data are in agreement with those reported previously in the literature.[S12]

General procedure of CsF-catalyzed fluoroacylation of TFE with acyl fluorides 9.

Under N_2 atmosphere, acyl fluoride **1** (0.500 mmol) was dissolved in DMF (2.50 mL) as a solvent. After addition of CsF (3.8 mg, 0.025 mmol) to a pressure-tight tube as a reactor (Wilmad-LabGlass, 513-7PVM-9; total volume is 12 mL), the solution was transferred to the tube. Then, TFE (1.5 atm, > ca. 1.1 eq) was charged into the reactor. The reaction mixture was heated at 140 °C for 4 h. After remaining TFE was purged from the reactor, the reaction mixture was quenched with water (10 mL). The resulting mixture was extracted with Et_2O (10 mL) three times. The combined organic phase was dried over Na_2SO_4. And then, the solvents were removed under reduced pressure. The crude material was purified by silica gel column chromatography (hexane/AcOEt = 97:3) to give the pentafluoroethyl ketone **11**. As for these compounds **11a**, **11e**, **11h**, and **11l**–**11o**, we present only NMR data in this section.

Characterization of pentafluoroethyl ketone 11.



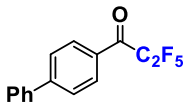
Pentafluoroethyl phenyl ketone (11a)

The reaction was performed with acyl fluoride **9a** (124 mg, 0.999 mmol). The title compound **11a** was detected in 95% yield. The yield was determined by the ^{19}F NMR measurement of the crude material using an internal standard. The product **11a** could not be isolated because the ketone **11a** was easily hydrated during purification by purification process using a silica-gel chromatography.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.09 (dd, J = 8.4, 1.2 Hz, 2H), 7.71 (t, 7.4 Hz, 1H), 7.55 (t, J = 8.0 Hz, 2H). **^{19}F NMR (DMF/$CDCl_3$, 376 MHz)**: δ = –84.3 (s, 3F), –118.2 (s, 2F).

GC-MS (EI): *m/z* $[M]^+$ calcd for $C_9H_5F_5O$: 224.0261; Found: 224.

The analytical data are in agreement with those reported previously in the literature.[S13]

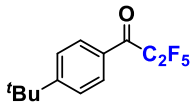


Pentafluoroethyl 4-biphenyl ketone (11b)

The reaction was performed with acyl fluoride **9b** (100 mg, 0.499 mmol). The title compound **11b** was isolated in 75% yield as a white solid (112 mg, 0.373 mmol). A gram-scale reaction was also performed with acyl fluoride **9b** (1.20 g, 6.00 mmol). The ketone **11b** was isolated in 69% yield (1.25 g, 4.16 mmol).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.18 (d, *J* = 8.4 Hz, 2H), 7.78–7.76 (m, 2H), 7.67–7.65 (m, 2H), 7.54–7.44 (m, 3H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = –84.2 (s, 3F), –118.1 (s, 2F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 182.7 (t, *J* = 26.7 Hz), 148.2 (s), 139.1 (s), 130.7 (t, J_{CF} = 3.3 Hz), 129.6 (s), 129.1 (s), 128.9 (s), 127.6 (s), 127.3 (s), 118.1 (qt, *J* = 286.8, *J* = 33.7 Hz, -*C*F_3), 108.8 (tq, *J* = 268.8, *J* = 37.2 Hz, -*C*F_2-). HRMS (EI): *m/z* $[M]^+$ calcd for $C_{15}H_9F_5O$: 300.0574; Found: 300.0576.

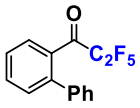
The analytical data are in agreement with those reported previously in the literature.[S14]



Pentafluoroethyl 4-*tert*-butylphenyl ketone (11c)

The reaction was performed with acyl fluoride **9c** (87.1 mg, 0.483 mmol). The title compound **11c** was isolated in 78% yield as a colorless oil (105 mg, 0.375 mmol).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.04 (d, *J* = 8.7 Hz, 2H), 7.56 (d, *J* = 8.7 Hz, 2H), 1.36 (s, 9H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = –84.3 (s, 3F), –118.2 (s, 2F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 182.7 (t, *J* = 26.5 Hz), 159.8 (s), 130.2 (t, *J* = 3.1 Hz), 128.4 (s), 126.1 (s), 118.1 (qt, *J* = 286.7, *J* = 33.8 Hz), 108.8 (tq, *J* = 268.7, *J* = 37.1 Hz), 35.5 (s), 30.9 (s). HRMS (EI): *m/z* $[M]^+$ calcd for $C_{13}H_{13}F_5O$: 280.0887; Found: 280.0889.

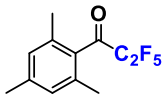


Pentafluoroethyl 2-biphenyl ketone (11d)

The reaction was performed with acyl fluoride 9**d** (100 mg, 0.499 mmol). The yield of the title compound **11d** was determined by the ^{19}F NMR measurement of the crude material using an internal standard (17% NMR). The title compound **11d** was isolated in 9% yield as a colorless oil (14.2 mg, 0.0473 mmol).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.65 (dd, *J* = 7.7 Hz, 2H), 7.50 (dd, *J* = 7.1 Hz, 2H), 7.45–7.38 (m, 3H), 7.30–7.28 (m, 2H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = –84.2 (s, 3F), –120.1 (s, 2F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 189.7 (t, *J* = 27.5 Hz), 142.8 (s), 139.6 (s), 133.3 (s), 132.5 (s), 131.0 (s), 128.8 (s), 128.6 (s), 128.3 (t, *J* = 2.7 Hz), 128.1 (s), 127.3 (s), 118.0 (qt, *J* = 287.6, *J* = 34.5 Hz), 107.2 (tq, *J* = 269.0, *J* = 37.3 Hz).

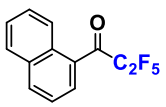
HRMS (EI): *m/z* $[M]^+$ calcd for $C_{15}H_9F_5O$: 300.0574; Found: 300.0570.



Pentafluoroethyl 2,4,6-trimethylphenyl ketone (11e)

The reaction was performed with acyl fluoride **9e** (83.1 mg, 0.500 mmol). The yield of the title compound **2e** was determined by the ^{19}F NMR measurement of the crude material using an internal standard (13% NMR).

^{19}F NMR (DMF/$CDCl_3$, 376 MHz): δ = –83.7 (s, 3F), –122.3 (s, 2F).



Pentafluoroethyl 1-naphthyl ketone (11f)

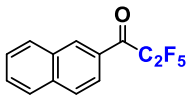
The reaction was performed with acyl fluoride **9f** (87.1 mg, 0.500 mmol). The title compound **11f** was isolated in 79% yield as a yellow oil (109 mg, 0.398 mmol).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.56 (d, *J* = 8.7 Hz, 1H), 8.17–8.13 (m, 2H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.68 (ddd, *J* = 7.7, 7.0, 1.5 Hz, 1H), 7.63-7.55 (m, 2H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = –83.9 (s, 3F), –117.2 (s, 2F). **^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz)**: δ = 185.8 (t, *J* = 25.8 Hz),

135.6 (s), 133.9 (s), 130.9 (s), 130.4 (t, J = 6.1 Hz), 129.3 (s), 128.9 (s), 128.1 (s), 127.1 (s), 124.9 (s), 124.1 (s), 118.3 (qt, J = 287.3, J = 34.1 Hz), 107.0 (tq, J = 270.7, J = 36.8 Hz).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{13}H_7F_5O$: 274.0417; Found: 274.0418.

The analytical data are in agreement with those reported previously in the literature.[S15]

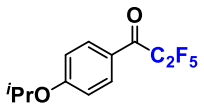


Pentafluoroethyl 2-naphthyl ketone (11g)

The reaction was performed with acyl fluoride **9g** (87.1 mg, 0.500 mmol). The yield of the title compound **11g** was determined by the ^{19}F NMR measurement of the crude material using an internal standard (67% NMR). The title compound **11g** was isolated in 48% yield as a yellow oil (65.8 mg, 0.240 mmol).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.66 (s, 1H), 8.07 (d, J = 8.7 Hz, 1H), 8.01 (d, J = 8.2 Hz, 1H), 7.94 (d, J = 8.8 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.69 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 7.61 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = –84.2 (s, 3F), –117.5 (s, 2F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 183.0 (t, J = 26.6 Hz), 136.4 (s), 133.2 (t, J_{CF} = 4.5 Hz), 132.1 (s), 130.3 (s), 130.1 (s), 129.0 (s), 128.2 (s), 127.9 (s), 127.4 (s), 124.2 (s), 118.1 (qt, J = 286.8, J = 33.8 Hz), 108.9 (tq, J = 268.9, J = 37.1 Hz). HRMS (EI): *m/z* $[M]^+$ calcd for $C_{13}H_7F_5O$; 274.0417; Found: 274.0413.

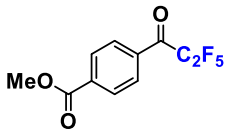
The analytical data are in agreement with those reported previously in the literature.[S16]



Pentafluoroethyl 4-isopropoxyphenyl ketone (11h)

The reaction was performed with acyl fluoride **9h** (91.1 mg, 0.500 mmol). The yield of the title compound **11h** was determined by the ^{19}F NMR measurement of the crude material using an internal standard (40% NMR). The product **11h** could not be isolated because the ketone **11h** was easily hydrated by purification process using a silica-gel chromatography.

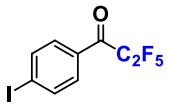
^{19}F NMR (DMF/$CDCl_3$, 376 MHz): δ = –84.5 (s, 3F), –117.9 (s, 2F).



Methyl 4-(pentafluoropropanoyl)benzoate (11i)

The reaction was performed with acyl fluoride **9i** (90.3 mg, 0.496 mmol). The yield of the title compound **11i** was determined by the ^{19}F NMR measurement of the crude material using an internal standard (67% NMR). The title compound **11i** was isolated in 52% yield as a yellow oil (72.5 mg, 0.257 mmol).

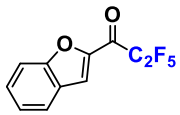
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.19 (d, *J* = 8.0 Hz, 2H), 8.14 (d, *J* = 8.0 Hz, 2H), 3.98 (s, 3H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = –84.2 (s, 3F), –118.5 (s, 2F). **$^{13}C\{^{1}H\}$ NMR ($CDCl_3$,100 MHz)**: δ = 182.9 (t, *J* = 27.3 Hz), 165.6 (s), 135.9 (s), 134.0 (s), 130.1 (s), 130.0 (t, *J* = 3.1 Hz), 117.9 (qt, *J* = 286.8, *J* = 33.1 Hz), 108.5 (tq, *J* = 269.1, *J* = 37.3 Hz), 52.7 (s). HRMS (EI): *m/z* $[M]^+$ calcd for $C_{11}H_7F_5O_3$: 282.0315; Found: 282.0315.



Pentafluoroethyl 4-iodophenyl ketone (11j)

The reaction was performed with acyl fluoride **9j** (125 mg, 0.500 mmol). The title compound **11j** was isolated by preparative HPLC in 54% yield as an orange oil (94.5 mg, 0.270 mmol).

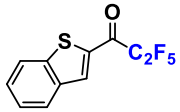
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.93 (d, *J* = 8.7 Hz, 2H), 7.77 (d, *J* = 8.6 Hz, 2H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = –84.8 (s, 3F), –118.9 (s, 2F). **$^{13}C\{^{1}H\}$ NMR ($CDCl_3$,100 MHz)**: δ = 182.7 (t, *J* = 27.1 Hz), 138.6 (s), 131.2 (t, *J* = 3.2 Hz), 130.2 (s), 117.9 (qt, *J* = 286.7, *J* = 33.5 Hz,), 108.5 (tq, *J* = 270.3, *J* = 36.7 Hz), 104. 7 (s). HRMS (EI): *m/z* $[M]^+$ calcd for $C_9H_4F_5IO$: 349.9227; Found: 349.9224.



2-Benzofuranyl pentafluoroethyl ketone (11k)

The reaction was performed with acyl fluoride **9k** (82.1 mg, 0.500 mmol). The title compound **11k** was isolated in 56% yield as a yellow oil (73.9 mg, 0.280 mmol).

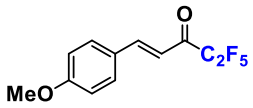
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.88 (s, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.65–7.58 (m, 2H), 7.39 (ddd, *J* = 8.0, 6.6, 1.2 Hz, 1H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = –84.4 (s, 3F), –121.6 (s, 2F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 172.7 (t, *J* = 27.4 Hz), 156.7 (s), 147.2 (s), 130.8 (s), 126.4 (s), 124.8 (s), 124.3 (s), 120.6 (t, J_{CF} = 5.5 Hz), 117.8 (qt, *J* = 287.2, *J* = 34.1 Hz), 112.7 (s), 108.1 (tq, *J* = 266.4, *J* = 38.3 Hz). HRMS (EI): *m/z* $[M]^+$ calcd for $C_{11}H_5F_5O_2$: 264.0210; Found: 264.0211.



2-Benzothiophenyl pentafluoroethyl ketone (11l)

The reaction was performed with acyl fluoride **9l** (90.1 mg, 0.500 mmol). The yield of the title compound **11l** was determined by the ^{19}F NMR measurement of the crude material using an internal standard (9% NMR).

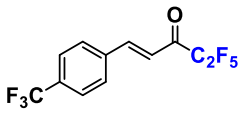
^{19}F NMR (DMF/$CDCl_3$, 376 MHz): δ = –84.3 (s, 3F), –119.4 (s, 2F).



(*E*)-4-Methoxycinnamyl pentafluoroethyl ketone (11m)

The reaction was performed with acyl fluoride **9m** (90.1 mg, 0.500 mmol). The yield of the title compound **11m** was determined by the ^{19}F NMR measurement of the crude material using an internal standard (21% NMR). The product **11m** could not be isolated because the ketone **11m** was easily hydrated by purification process using a silica-gel chromatography.

^{19}F NMR (DMF/$CDCl_3$, 376 MHz): δ = –85.0 (s, 3F), –126.4 (s, 2F).



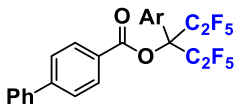
(*E*)-4-Trifluoromethylphenyl pentafluoroethyl ketone (11n)

The reaction was performed with acyl fluoride **9n** (109 mg, 0.500 mmol). The yield of the title compound **11n** was determined by the ^{19}F NMR measurement of the crude material using an internal standard (7% NMR).

^{19}F NMR (DMF/$CDCl_3$, 376 MHz): δ = –65.8 (s, 3F), –85.0 (s, 3F), –126.4 (s, 2F).

Stoichiometric reaction at 80 ºC and Isolation of ester 12b.

Biphenyl-4-carboxylic acid fluoride (**9b**, 100 mg, 0.499 mmol) was dissolved into DMF (2.50 mL) as a solvent. After addition of CsF (76.0 mg, 0.500 mmol) to a pressure-tight reaction vessel (total volume is 12 mL) as a reactor, the resulting solution was transferred to the tube. Then, TFE (2.5 atm) was charged into the reactor. The reaction mixture was heated at 80 °C for 2 h. After, the remaining TFE was purged from the reactor, the reaction mixture was quenched by addition of water (10.0 mL). The resulting mixture was extracted with ether (10 mL) three times. The solvents were removed under reduced pressure. The yields of the ketone **11b** and ester **12b** were estimated by ^{19}F NMR measurement of the crude material (**11b**: 13%, **12b**: 47%). The crude material was purified by preparative HPLC to give the corresponding ester **12b** as colorless oil in 38% yield (56.7 mg, 0.0944 mmol).



Ar: 4-Ph-C_6H_4

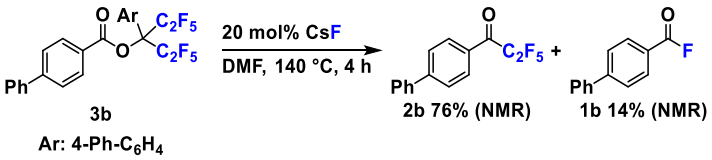
3-(4-Biphenyl)-1,1,1,2,2,4,4,5,5,5-decafluoropentyl biphenyl-4-carboxylate (12b):
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.22 (d, *J* = 8.3 Hz, 2H), 7.78 (d, *J* = 8.1 Hz, 2H), 7.69–7.62 (m, 6H), 7.55–7.46 (m, 7H), 7.40 (dd, *J* = 7.2, 7.2 Hz, 1H). **^{19}F NMR ($CDCl_3$, 376 MHz)**: δ = –80.2 (s, 3F), –80.3 (s, 3F), –110.6 (d, $^1J_{CF}$ = 295.4 Hz, 2F), –114.9 (d, $^1J_{CF}$ = 296.0 Hz, 2F). **^{13}C{^{1}H} NMR ($CDCl_3$,100 MHz)**: δ = 161.9 (s), 147.4 (s), 142.8 (s), 139.6 (s), 139.5 (s), 130.8 (s), 129.1 (s), 128.9 (s), 128.6 (s), 128.3 (s), 128.0 (s), 127.6 (s), 127.3 (s), 127.2 (s), 126.7 (s), 126.4 (s), 125.0 (s), 118.6 (qt, $^1J_{CF}$ = 289.8 Hz, $^2J_{CF}$ = 35.3 Hz, -*C*F_3), 113.2 (tq, $^1J_{CF}$ = 272.8 Hz, $^2J_{CF}$ = 37.7 Hz, -*C*F_2-), 86.3 (t, J_{CF} = 26.7 Hz). HRMS (EI): *m/z* $[M]^+$ calcd for $C_{30}H_{18}F_{10}O_2$: 600.1147; Found: 600.1146.

CsF-catalyzed fluoroacylation of HFP or TFE with acyl fluoride 9a at room temperature.

These reactions were performed according to the reported reaction conditions.[S17] Under N_2 atmosphere, benzoyl fluoride **9a** (0.500 g, 4.00 mmol) was dissolved to DMF (0.500 mL). After addition of CsF (50.0 mg, 0.330 mmol) to an autoclave reactor equipped with a stirrer bar, the solution was transferred to the reactor. Then, HFP or TFE (1.5 atm) was charged into the reactor. The reaction mixture was stirred at room temperature for 2 h. After the remaining gas was purged

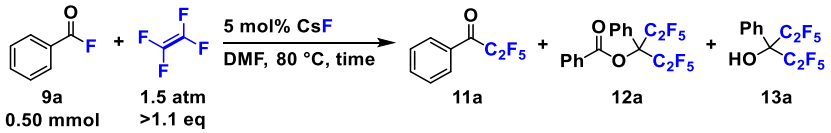
from the reactor, α,α,α-trifluorotoluene (100 μL, 0.815 mmol) was added as an internal standard. Yields were determined by ^{19}F NMR measurement of the crude materials respectively.

Investigation of reactivity of ester 12b under CsF catalytic system.



12b (30.0 mg, 0.0500 mmol) and α,α,α-trifluorotoluene (5.0 μL, 0.041 mmol) were dissolved to a mix solvent of DMF and C_6D_6 (0.500 mL, v/v' = 4/1). After addition of CsF (1.55 mg, 0.0102 mmol) to a pressure-tight NMR tube (Wilmad-LabGlass, 524-PV-7; total volume: 2 mL), the solution was transferred to the tube. The reaction tube was heated at 140 °C for 4 h. The yields of the ketone **11b** and acyl fluoride **9b** were determined by ^{19}F NMR measurement of the crude material using an internal standard.

Yield change of perfluoroalkylation of 1a at 80 °C over reaction time.



Under N_2 atmosphere, benzoyl fluoride (**1a**) (62.1 mg, 0.500 mmol) was dissolved into DMF (0.500 mL). After addition of CsF (3.8 mg, 0.025 mmol) to a pressure-tight tube (Wilmad-LabGlass 513-7PVM-9; total volume; 12 mL), the solution was transferred to the tube. After further addition of DMF (2.0 mL), TFE (1.5 atm, > ca. 1.1 eq) was charged into the reactors. The reaction mixtures were respectively heated at 80 °C for 2, 4, 8 or 20 h. After the unreacted gas was purged from the reactor, α,α,α-trifluorotoluene was added as an internal standard to each reaction mixture. The yields of **9a**, **11a**, **12a** and **13a** were determined by ^{19}F NMR measurement of the crude materials. The results are summarized in Table 4.S1 and Figure 4.S1.

Table 4.S1. Yields of each product at 80 °C.

time/h	**9a**/%	**11a**/% (max 100%)	**12a**/% (max 100%)	**13a**/% (max 100%)
0	100	0	0	0
2	67	21	10	0
4	37	27	30	<1
8	15	31	44	3
20	10	42	35	3

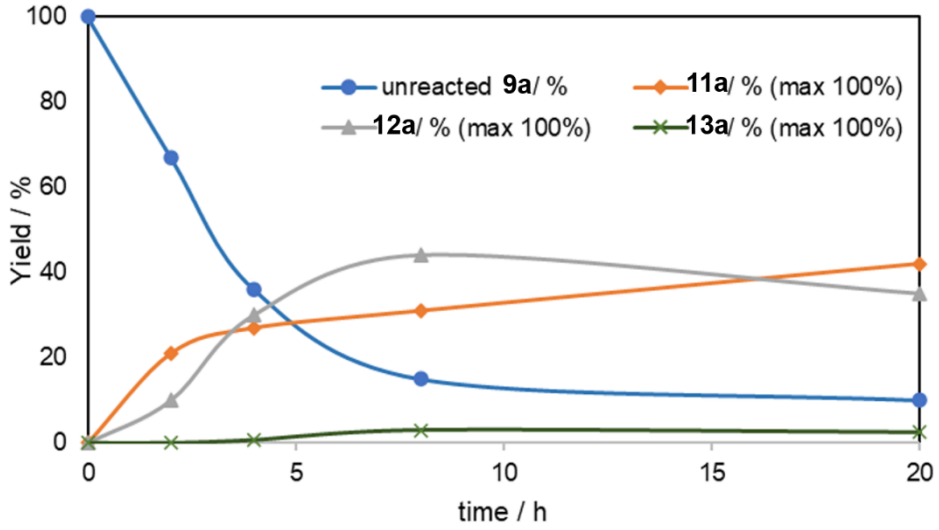


Figure 4.S1. Time-course change of yields at 80 °C.

Computational Study

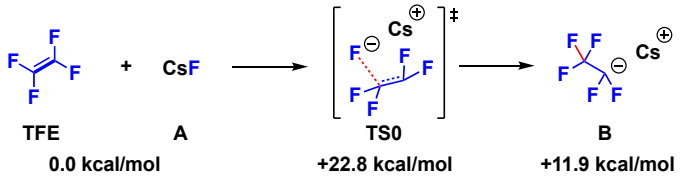
1. Calculation method details.

All geometry optimizations for the pentafluoroethylation reaction pathways using density functional theory (DFT) were performed with Gaussian 09 (revision D.01)[S18] suite of programs at B3LYP level[S19,S20] combined with Grimme's dispersion correlation[S21] of theory using SMD solvation model (ε = 37.219, DMF)[S22] and an effective core potential, Lanl2DZ[S23] for cesium atom and 6-31+G(d,p) as double-zeta quality basis sets. Harmonic frequency calculations were conducted at the same level of theory on the optimized geometries to check all the stationary points as either minima or first-order saddle points. Intrinsic reaction coordinate (IRC)[S24] calculations were carried out to confirm the transition states connecting the correct reactants and products on the potential energy surface. The thermal energy corrections were calculated for the optimized geometry at B3LYP level combined with Grimme's dispersion correlation of theory using SMD solvation model (ε = 37.219, DMF) and an effective core potential, SDD[S21] for cesium atom and 6-311++G(d,p) as triple-zeta quality basis sets.

Summary: B3LYP-D3/6-311++G(d,p), SDD for Cs atom/SMD(ε = 3.7219, DMF)//B3LYP-D3/6-31+G(d,p), Lanl2DZ for Cs/SMD(ε = 3.7219, DMF).

2. DFT calculation of formation of pentafluoroethyl cesium (B).

The calculation of the formation of pentafluoroethyl cesium (**B**) was conducted. The related Gibbs activation energy value of the transition state (TS0) of the nucleophilic attack of a fluoride anion of CsF (**A**) to a C–C double bond of TFE was reasonable to proceed at 140 ºC ($\Delta G^{‡}$ = +22.8 kcal/mol). This process was predicted as an endothermic step by the DFT calculation. The resulting pentafluoroethyl cesium (**B**) was highly unstable compared to CsF (**A**) and TFE [ΔG (**B**) = +11.9 kcal/mol]. This calculation was agreed with the experimental result which pentafluoroethyl cesium (**B**) was not observed in the reaction mixture.



Scheme 4.S1. DFT calculation of formation of pentafluoroethyl cesium (**B**).

3. Calculated Properties and Geometries

Table 4.S2. Calculated energies and thermochemical parameters of the optimized structures.

Structure	*E* [hartree]	*H* [hartree]	*TS* [hartree]	*G* [hartree]
413.15 K (140 ºC)				
TFE	-475.640608	-475.639300	0.053552	-475.692852
CsF (**A**)	-120.149357	-120.148049	0.042768	-120.190817
TS0	-595.79296	-595.775205	0.07309	-595.84732
CsC_2F_5 (**B**)	-595.792960	-595.791652	0.07309	-595.864742
PhCOF (**1a**)	-444.875649	-444.874340	0.061871	-444.936211
TS1	-1040.671781	-1040.670472	0.106168	-1040.776640
$PhCOC_2F_5$ (**2a**)	-920.554913	-920.553605	0.086189	-920.639794
TS2	-1516.351572	-1516.350264	0.128215	-1516.478479
$PhC(C_2F_5)_2OCs$ (**4a_Cs**)	-1516.384254	-1516.382946	0.122790	-1516.505736
TS3	-1961.244870	-1961.243562	0.150322	-1961.393884
$[PhC(C_2F_5)_2O]PhCO$ (**3a**)	-1841.108716	-1841.107408	0.137050	-1841.244458
TS4	-2436.902936	-2436.901628	0.175828	-2437.077456

353.15 K (80 ºC)				
TFE	-475.642498	-475.64138	0.043855	-475.685235
CsF (**A**)	-120.150021	-120.148903	0.035769	-120.184672
TS0	-595.779373	-595.778254	0.058828	-595.837082
CsC_2F_5 (**B**)	-595.795927	-595.794809	0.059562	-595.854371
PhCOF (**1a**)	-444.878841	-444.877722	0.049768	-444.927490
TS1	-1040.678331	-1040.677213	0.084532	-1040.761745
$PhCOC_2F_5$ (**2a**)	-920.560397	-920.559279	0.068439	-920.627718
TS2	-1516.360399	-1516.359281	0.101276	-1516.460557
$PhC(C_2F_5)_2OCs$(**4a_Cs**)	-1516.393081	-1516.391963	0.096640	-1516.488603
TS3	-1961.257250	-1961.256132	0.116899	-1961.373031
$[PhC(C_2F_5)_2O]PhCO$ (**3a**)	-1841.120089	-1841.118970	0.106485	-1841.225455
TS4	-2436.917643	-2436.916525	0.136553	-2437.053078
298.15 K (25 ºC)				
TFE	-475.644065	-475.643121	0.035416	-475.678537
CsF (**A**)	-120.150629	-120.149685	0.029480	-120.179165
TS0	-595.781838	-595.780893	0.047246	-595.828139
CsC_2F_5 (**B**)	-595.798425	-595.797481	0.047778	-595.845259
PhCOF (**1a**)	-444.881280	-444.880336	0.039678	-444.920014
TS1	-1040.683694	-1040.682750	0.065956	-1040.748706
$PhCOC_2F_5$ (**2a**)	-920.564887	-920.563943	0.053160	-920.617103
TS2	-1516.367636	-1516.366692	0.078568	-1516.445260
$PhC(C_2F_5)_2OCs$(**4a_Cs**)	-1516.400312	-1516.399367	0.074858	-1516.474225
TS3	-1961.267306	-1961.266362	0.089420	-1961.355782
$[PhC(C_2F_5)_2O]PhCO$ (**3a**)	-1841.129197	-1841.128252	0.081396	-1841.209648
TS4	-2436.929679	-2436.928735	0.104100	-2437.032835

TFE

C	-0.662643	-0.000397	-0.000077
F	-1.392767	1.108786	-0.000194
C	0.661841	-0.000356	0.000103
F	-1.393397	-1.108834	-0.000193
F	1.394049	-1.108379	0.000185
F	1.392649	1.108930	0.000184

CsF (**A**)

F	0.000000	0.000000	-2.739658
Cs	0.000000	0.000000	0.448308

TS0

C	2.048771	-0.485255	0.236685
C	2.149840	0.895478	0.303697
F	1.005250	1.569752	0.670165

F	2.695645	1.522857	-0.790404
F	3.115742	-1.164928	-0.185965
F	1.438840	-1.107148	1.250178
Cs	-1.955687	0.005731	-0.037216
F	0.896867	-1.129037	-1.076799

CsC_2F_5 (**B**)

C	-1.798825	0.912126	0.057475
C	-2.156298	-0.567915	-0.008458
Cs	2.375354	0.034717	0.007557
F	-2.463610	1.438090	-1.112031
F	-2.653345	1.384320	1.121272
F	-1.715878	-1.217033	1.106429
F	-1.554557	-1.159720	-1.078856
F	-3.491914	-0.887288	-0.115675

PhCOF (**9a**)

C	-1.698317	-0.146081	-0.000017
O	-2.391997	-1.123351	-0.000178
C	-0.232402	-0.046939	0.000100
C	0.425755	1.195486	-0.000019
C	0.508101	-1.243379	0.000137
C	1.819965	1.235160	-0.000035
H	-0.147301	2.115534	-0.000071
C	1.900183	-1.193508	0.000013
H	-0.011569	-2.195957	0.000270
C	2.556131	0.044604	-0.000068
H	2.331642	2.192743	-0.000059
H	2.474285	-2.115029	0.000015
H	3.641871	0.080804	-0.000176
F	-2.314383	1.092962	0.000087

TS1

C	-1.709486	2.223700	-0.440246
O	-2.152352	2.432464	-1.537080
C	-0.299278	2.287376	0.003040
C	0.680021	2.579445	-0.961288
C	0.066181	2.127909	1.349897
C	2.015729	2.716380	-0.578809
H	0.387140	2.704054	-1.998991
C	1.403854	2.262771	1.725631
H	-0.689718	1.895222	2.091672
C	2.379278	2.562422	0.765236
H	2.770431	2.944829	-1.325948
H	1.685376	2.138276	2.767415
H	3.418754	2.670512	1.062760
F	-2.596661	2.177468	0.631161
Cs	2.177985	-1.306392	-0.199512
C	-1.846609	-0.535910	-0.523867
C	-2.000590	-1.550788	0.598947
F	-3.070037	-0.677752	-1.250840
F	-0.896320	-1.179072	-1.403707
F	-2.993750	-1.176167	1.449494
F	-0.852687	-1.626037	1.335561
F	-2.287980	-2.851873	0.242958

$PhCOC_2F_5$ (**11a**)

C	-0.060402	0.690935	0.000455
O	0.325770	1.849251	0.000879
C	-1.480624	0.284853	0.000018
C	-2.445296	1.313914	-0.000217
C	-1.900525	-1.060204	0.000029

C	-3.801177	1.003053	-0.000506	C	0.347019	-1.301142	1.388996
H	-2.117238	2.347982	-0.000172	C	-0.593555	-2.487080	1.220226
C	-3.261970	-1.363782	-0.000241	F	1.637407	-1.930176	1.371067
H	-1.184689	-1.872480	0.000199	F	0.188438	-0.981359	2.785961
C	-4.211832	-0.337176	-0.000552	F	-0.516165	-2.984697	-0.046199
H	-4.538797	1.799931	-0.000698	F	-1.889789	-2.105471	1.417881
H	-3.579842	-2.401823	-0.000232	F	-0.403873	-3.568567	2.052441
H	-5.270848	-0.579107	-0.000816	C	1.221169	2.000359	0.440541
C	1.034212	-0.422449	0.000893	C	-0.110102	2.718512	0.815010
C	2.497888	0.103830	-0.000743	F	1.727128	1.475665	1.587492
F	0.904423	-1.217602	1.106695	F	2.084723	2.993389	0.033432
F	0.903946	-1.220590	-1.103155	F	0.110009	3.533750	1.867867
F	2.749449	0.840046	1.093418	F	-0.566306	3.471086	-0.199146
F	2.747831	0.837179	-1.097075	F	-1.064467	1.839543	1.165990
F	3.345863	-0.946406	0.000103	PhC(C_2F_5)$_2$OCs (**13a_Cs**)			
				C	0.829525	0.208436	0.009643
TS2				O	-0.235988	-0.129168	-0.708602
C	1.107712	0.964337	-0.719154	C	2.204342	-0.047649	-0.694126
O	0.107914	1.037989	-1.423438	C	2.166514	-0.669617	-1.945978
C	2.264651	0.095107	-1.017177	C	3.446070	0.335295	-0.163998
C	2.082979	-0.905576	-1.992332	C	3.345366	-0.924794	-2.654768
C	3.522219	0.245060	-0.403245	H	1.195777	-0.947668	-2.343761
C	3.135391	-1.747428	-2.338270	C	4.627233	0.085379	-0.870806
H	1.109334	-1.020590	-2.457588	H	3.502668	0.836808	0.796375
C	4.577394	-0.595348	-0.763076	C	4.581901	-0.549066	-2.118140
H	3.694646	1.009978	0.344055	H	3.297797	-1.413853	-3.624740
C	4.386523	-1.593922	-1.723425	H	5.581247	0.389964	-0.447875
H	2.985141	-2.524401	-3.082257	H	5.500137	-0.744129	-2.666250
H	5.546889	-0.470827	-0.289757	Cs	-3.207587	-0.592779	-0.813135
H	5.208413	-2.251042	-1.993908	C	0.805959	-0.604812	1.376638
Cs	-2.960365	-0.056232	-1.071140	C	0.528074	-2.132335	1.198807

F	1.963345	-0.520479	2.120894	H	-2.482055	-1.723156	0.229781
F	-0.197763	-0.165663	2.207806	C	-0.836606	-4.801744	-1.461004
F	1.324121	-2.692263	0.271111	H	0.194928	-3.356100	-2.698612
F	-0.751242	-2.392359	0.877643	C	-1.750443	-4.985474	-0.417922
F	0.770347	-2.768470	2.374080	H	-3.056516	-4.004488	0.997782
C	0.763822	1.768449	0.352630	H	-0.371255	-5.660870	-1.937182
C	-0.663192	2.413580	0.374611	H	-1.999102	-5.987704	-0.078793
F	1.362713	2.104142	1.549168	C	2.141995	-0.618016	-0.438337
F	1.418623	2.496955	-0.614210	C	3.473394	-0.743806	0.384498
F	-0.556115	3.679581	0.859411	C	1.151359	1.747703	-0.780340
F	-1.188418	2.512878	-0.859404	C	0.231972	2.163285	-1.750687
F	-1.544065	1.769883	1.156880	C	2.218096	2.599681	-0.453000
				C	0.380056	3.398393	-2.390293
TS3				H	-0.595281	1.519202	-2.010842
C	0.919793	0.384689	-0.071233	C	2.364623	3.835493	-1.090312
O	-0.294103	-0.205407	-0.344128	H	2.939340	2.321949	0.303232
C	0.786603	0.673221	1.471837	C	1.447323	4.240868	-2.064867
C	0.160278	-0.460385	2.360769	H	-0.343025	3.698608	-3.144217
F	1.975357	1.025751	2.050100	H	3.197425	4.478960	-0.819569
F	-0.047559	1.748754	1.642329	H	1.562062	5.200804	-2.561147
F	0.635160	-1.675039	2.053193	F	2.573969	-0.320273	-1.701488
F	-1.180046	-0.486457	2.267368	F	1.668096	-1.895041	-0.458702
F	0.461392	-0.215804	3.657387	F	4.279236	-1.623385	-0.251854
C	-0.729550	-1.024321	-1.810295	F	3.261431	-1.222088	1.622327
Cs	-3.167622	1.604546	0.402403	F	4.146455	0.415584	0.478084
F	-2.047481	-0.277118	-1.931659				
O	0.026661	-0.836750	-2.746804	[PhC(C_2F_5)$_2$O]PhCO (**12a**)			
C	-1.107138	-2.394084	-1.288823	C	0.546757	-0.075912	0.061644
C	-2.026290	-2.581329	-0.247682	O	-0.866102	-0.148211	-0.098588
C	-0.517186	-3.509888	-1.893983	C	0.995348	1.126840	0.902047
C	-2.345256	-3.869937	0.186851	C	0.096901	2.181620	1.118030

C	2.308000	1.240206	1.378835	H	-2.716975	-0.174853	-1.625308
C	0.499458	3.319922	1.818022	C	-5.832761	-0.366501	-0.267476
H	-0.915700	2.137534	0.735027	H	-6.264903	-0.523086	1.844220
C	2.708717	2.382233	2.075912	H	-5.099862	-0.207214	-2.292904
H	3.031287	0.452634	1.218543	H	-6.877955	-0.380179	-0.563382
C	1.806463	3.424816	2.301424				
H	-0.212108	4.124200	1.979213	**TS4**			
H	3.728959	2.450012	2.441555	C	1.477880	0.145182	0.132466
H	2.119219	4.310788	2.846344	O	0.451743	1.117126	0.181531
C	0.992753	0.104179	-1.431579	C	1.152347	-1.150294	0.892867
C	0.574168	1.425721	-2.168631	C	0.105606	-1.120377	1.822100
F	2.353281	0.067059	-1.509162	C	1.896867	-2.329581	0.743593
F	0.496857	-0.918690	-2.182324	C	-0.208820	-2.253095	2.575926
F	1.259192	2.480141	-1.698961	H	-0.465435	-0.214410	1.956996
F	-0.736954	1.681113	-2.065395	C	1.579264	-3.464079	1.496716
F	0.873500	1.286549	-3.475379	H	2.719957	-2.392324	0.046285
C	1.050073	-1.502982	0.646631	C	0.522624	-3.433274	2.412397
C	2.345449	-2.252930	0.150391	H	-1.031210	-2.208415	3.284376
F	1.223345	-1.393498	1.988880	H	2.159882	-4.371937	1.359759
F	0.057472	-2.411502	0.422231	H	0.275464	-4.317937	2.992771
F	2.260982	-2.605260	-1.139657	C	2.635560	0.925587	0.847880
F	3.467873	-1.541670	0.337002	C	2.434260	1.348128	2.344586
F	2.455383	-3.383060	0.877053	F	3.774445	0.170964	0.838887
O	-1.363309	-0.447742	2.102485	F	2.894698	2.083398	0.174660
C	-1.736262	-0.323434	0.957749	F	2.386319	0.278418	3.155128
C	-3.142879	-0.332093	0.491614	F	1.333784	2.084917	2.532790
C	-4.148565	-0.432038	1.468375	F	3.502184	2.090784	2.708376
C	-3.488776	-0.249916	-0.868476	C	1.869664	-0.123106	-1.420287
C	-5.489363	-0.447468	1.087853	C	3.344777	-0.310062	-1.947265
H	-3.870019	-0.495210	2.515156	F	1.222865	-1.241095	-1.854190
C	-4.832986	-0.268539	-1.242071	F	1.416891	0.932430	-2.155367

F	4.083869	0.796165	-1.787550
F	3.983904	-1.343663	-1.377751
F	3.267580	-0.561516	-3.270745
O	-1.108525	-0.083149	-1.000058
C	-0.758484	0.998508	-0.548909
C	-1.162061	2.322052	-1.112319
C	-2.224370	2.346510	-2.028329
C	-0.506547	3.517173	-0.779665
C	-2.639628	3.554589	-2.591585
H	-2.722923	1.417480	-2.283497
C	-0.921332	4.723930	-1.348528
H	0.319100	3.502848	-0.077336
C	-1.989849	4.748358	-2.252942
H	-3.465875	3.564790	-3.297625
H	-0.408219	5.645587	-1.086984
H	-2.312170	5.688983	-2.691432
Cs	-1.777733	-3.139310	-1.101504
C	-2.309154	1.383857	1.307839
C	-3.469085	0.403962	1.184407
F	-1.915691	1.280945	2.672341
F	-2.927886	2.656003	1.253178
F	-4.484160	0.550310	2.105955
F	-4.060230	0.506844	-0.032297
F	-3.035919	-0.876932	1.319024

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Conclusion

Described in this thesis were the studies on synthesis of fluoroalkyl compounds via addition of metal species to TFE. The studies enable efficient and straightforward transformations of TFE into more organofluorine compounds without using high cost and hazardous reagents.

In Chapter 2, the copper-mediated one-pot synthesis of *N*-tetrafluoroethylated heteroarenes was described. A variety of 2-aryl-1-heteroaryl-1,1,2,2-tetrafluoroethane were prepared directly from tetrafluoroethylene and sodium imidazolides and iodoarenes. This is an environmentally benign reaction because it does not require Halon-2402, which is an already banned material.

In Chapter 3 the catalytic synthesis of pentafluoroethyl arenes was described. The fluorocupration of TFE gave the pentafluoroethyl copper species. In addition, it was crucial to refrain stirring for the synthesis of pentafluoroethyl arenes in high yield. this reaction would serve as a cost-effective synthetic route for the synthesis of pentafluoroethyl arenes.

In Chapter 4, the catalytic synthesis of pentafluoroethyl ketones was described. Mechanistic studies suggest that a high temperature would furnish the thermodynamically favored ketone as the main product.

These results suggest that the addition of metal species to TFE would serve as a precursor for the introduction of fluoroalkyl groups into organic compounds. Thus, the studies in this thesis will provide new strategies of the synthesis of organofluorine compounds in organic synthesis. In addition, I believe that these studies will give a significant development in the field of pharmaceutical sciences.

List of Publications

1. Copper(I)-Mediated C–N/C–C Bond-Forming Reaction with Tetrafluoroethylene for the Synthesis of N-Fluoroalkyl Heteroarenes via an Azacupration/Coupling Mechanism
   Naoyoshi Ishida, Takuya Adachi, Hiroaki Iwamoto, Masato Ohashi, Sensuke Ogoshi
   Chem. Lett. **2020**, *accepted* (DOI:10.1246/cl.200903).

2. Cu^{I}-Catalyzed Pentafluoroethylation of Aryl Iodides in the Presence of Tetrafluoroethylene and Cesium Fluoride: Determining the Route to the Key Pentafluoroethyl Cu^{I} Intermediate
   Masato Ohashi, Naoyoshi Ishida, Kota Ando, Yu Hashimoto, Anna Shigaki, Kotaro Kikushima, Sensuke Ogoshi
   Chem. Eur. J. **2018**, *24,* 9794–9798.

3. CsF-Catalyzed Fluoroacylation of Tetrafluoroethylene Using Acyl Fluorides for the Synthesis of Pentafluoroethyl Ketones
   Naoyoshi Ishida, Hiroaki Iwamoto, Denise Eimi Sunagawa, Masato Ohashi, Sensuke Ogoshi
   Synthesis **2020**, *accepted eFirst Article* (DOI:10.1055/s-0040-1705962).

Supplementary Publications

1. Synthesis and Reactivity of Fluoroalkyl Copper Complexes by the Oxycuprationof Tetrafluoroethylene
   Masato Ohashi, Takuya Adachi, Naoyoshi Ishida, Kotaro Kikushima, Sensuke Ogoshi
   Angew. Chem. Int. Ed. **2017**, *56,* 11911-11915.