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Fluorine–copper exchange reaction of α,β,γ,γ,γ-pentafluorocrotonates with organocuprates: Generation and cross-coupling reactions of β-metallated α,γ,γ,γ-tetrafluorocrotonates

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ABSTRACT

Reaction of α,β,γ,γ,γ-pentafluorocrotonates with organocuprates derived from organomagnesium or zinc reagents in THF at −78 °C for 1 h took place smoothly to generate β-metallated intermediate, of which hydrolysis gave the β-reduction product in good yield. The fluorinated vinylcopper intermediate formed by fluorine–copper exchange was found to be stable at low temperature due to the strong electron-withdrawing effect of a CF_3 group, and was readily converted to various types of β-substituted products in good yields with high stereoselectivity by treating with electrophiles, such as iodine and allylic bromides.

1. Introduction

Selective C–F bond-cleavage reactions have become important transformations as well as C–F bond-forming reactions in organic chemistry [1]. Recently, C–C bond-forming reactions involving the C–F bond-cleavage have been reported by several groups [2]. Out of the C–F bond-cleavage reactions, addition–elimination reaction of fluorinated alkenes is recognized as one of the most convenient and powerful protocols for the transformation of a C–F bond to other C–X bonds (X = C [3], O [4], S [5], N [6], *etc.*) (Scheme 1).

Fluorine-substituted α,β-unsaturated carbonyl compounds are highly promising substrates for the addition-elimination reactions to afford various types of organofluorine compounds [7] as well as fluorine-containing materials [8]. Among such compounds, we recently reported that the reaction of some vinyl fluorides, such as perfluorocyclopentene, α,β,β-trifluoroacrylic ester, and α,β,β-trifluorovinyl sulfone, with organometallic reagents proceeded smoothly to give the corresponding addition–elimination products with high stereoselectivity [9]. During the course of our continuous studies, we found a synthetic strategy for 1,3,3,3-tetrafluoroprop-1-en-2-ylcopper species involving *fluorine–copper exchange reaction* of α,β,γ,γ,γ-pentafluoroprop-1-ene compounds bearing an electron-withdrawing group with organocopper reagents [9,10]. In this paper, we wish to describe this *fluorine–copper exchange reaction* of α,β,γ,γ,γ-pentafluorocrotonates with various organocuprates derived from organomagnesium or zinc reagents in detail (Scheme 2). In addition is also described the subsequent cross-coupling reaction of the vinylcopper intermediates with various electrophiles, leading to the efficient preparation of tetra-substituted alkenes.

2. Results and discussion

2.1. Reaction of α,β,γ,γ,γ-pentafluorocrotonates with organocuprates derived from Grignard reagents

Initially, the reaction of α,β,γ,γ,γ-pentafluorocrotonates **1** with freshly prepared phenylmagnesium bromide (**5a**) in the absence or presence of copper(I) salt was examined and the results are summarized in Table 1. The starting crotonates **1** were prepared from commercially available perfluorobutanoic acid in 3 steps with a slight modification of the reported procedure [11], as described in Section 4.

Thus, the treatment of benzyl α,β,γ,γ,γ-pentafluorocrotonate (**1A**) with **5a** without any additive in THF at −78 °C for 1 h, followed by hydrolysis, did not lead to any products (entry 1). As shown in entries 2 and 3, CuBr and CuI were not the additive of choice for the present reaction, the starting crotonate being recovered in high yield. On the other hand, the use of CuCN was somewhat effective, providing the β-reduction product **2A** in 34% yield after hydrolysis (entry 4). Quite interestingly, any trace of the addition–elimination product **4Aa** was not detected at all in this

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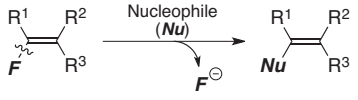


Scheme 1. C–F bond-cleavage involving addition–elimination reaction on fluorinated alkenes.

case [12]. Either prolonged reaction time (20 h) or raising reaction temperature (−20 °C) did not cause any improvement on the yield of **2A**, while the formation of benzyl 4,4,4-trifluoro-2-butynoate was observed (entries 5 and 6). Eventually, it was found that the reaction of **1A** with 2.2 equiv. of organocuprate, prepared from CuCN (2.2 equiv.) and **5a** (4.4 equiv.), in THF at −78 °C for 1 h proceeded smoothly to give the corresponding β-reduction product **2A** in 66% (50% isolated) yield as a sole stereoisomer, together with benzyl γ,γ,γ-trifluoro-β-phenylcrotonate (**3Aa**) in 18% yield (entry 7). The use of hexamethylphosphoric triamide (HMPA) or *N,N*-dimethylformamide (DMF) as an additive[13] did not cause significant change in the yield of **2A** (entries 8 and 9). The reaction at higher temperature (−20 °C) gave **3Aa** in 80% (79% isolated) yield as a mixture of the *E*/*Z* isomers (*E*/*Z* = *ca.* 50/50) (entry 10). Other fluorinated substrates **1B** and **1C** also underwent the similar reaction to yield the corresponding β-reduction product **2B** or **2C** in 64% (50% isolated) or 55% (42% isolated) yield, respectively (entries 11 and 12).

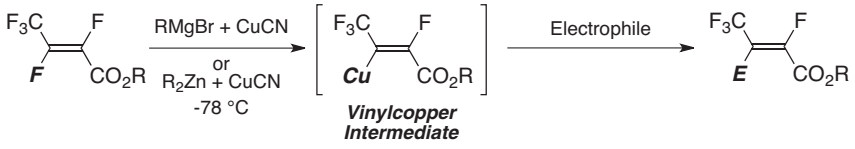
Subsequently, various Grignard reagents were applied to the reaction with fluorinated crotonate **1A** in order to verify the generality of the Grignard reagent. Thus, the reaction of **1A** with 2.2 equiv. of organocuprate, derived from CuCN (2.2 equiv.) and Grignard reagent **5** (4.4 equiv.), in THF at −78 °C for 1 h, followed by treating a saturated aqueous NH_4Cl solution, was carried out. The results are tabulated in Table 2.

Aryl Grignard reagents bearing an electron-donating group, like 4-methoxy- (**5b**), 3-methoxy- (**5c**), and 4-methylphenylmagnesium bromide (**5e**), also took part well in the reaction to afford the corresponding β-reduction product **2A** in 61–65% (50–56% isolated) yields (entries 2, 3, and 5). On the contrary, aryl Grignard reagents having either a substituent at the 2-position on benzene ring or an electron-withdrawing group, such as 2-methoxy- (**5d**) or 4-(trifluoromethyl)phenylmagnesium bromide (**5f**), were not suitable nucleophiles, giving the β-reduction product **2A** in only 23% or 27% yield, respectively (entries 4 and 6). *n*-Butyl- (**5 g**) and methylmagnesium bromide (**5 h**) reacted successfully with **1A** to produce **2A** in 59% (40% isolated) and 60% (38% isolated) yields, respectively (entries 7 and 8). Both secondary alkyl (**5i**) and vinyl Grignard reagents (**5j**) were turned out to be unreactive, a large amount of **1A** being recovered (entries 9 and 10).

Surprisingly, the use of allyl- (**5k**) or benzylmagnesium chloride (**5l**) as a Grignard reagent resulted in the addition–elimination product **4Ak** or **4Al** in 62% (*Z*/*E* = 68/32) or 51% (*Z*/*E* = 71/29) yield, respectively (Scheme 3). In these cases, any trace of the β-reduction product **2A** was not detected at all.

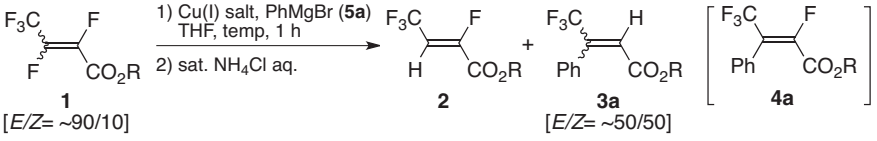
2.2. Reaction of α,β,γ,γ,γ-pentafluorocrotonates with organocuprate derived from dialkylzinc

Similarly, the reaction of the fluorinated crotonate **1A** with various organocuprates derived from organolithium or zinc reagents was conducted. The reaction of **1A** with 2.2 equiv. of organocuprate, prepared from CuCN (2.2 equiv.) and phenyllithium (4.4 equiv.), in THF at −78 °C for 1 h, followed by



Scheme 2. Successive fluorine–copper exchange/cross-coupling reaction sequence.

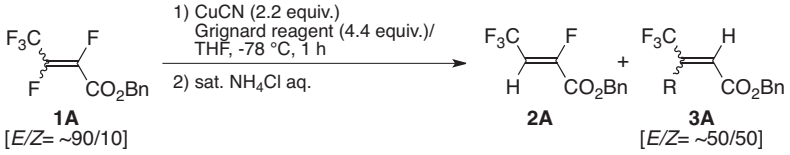
Table 1
Cu(I)-mediated addition–elimination reaction of **1** with PhMgBr (**5a**) .



Entry	Substrate (*R*)	Cu(I) salt/equiv.	Equiv. of PhMgBr (5a)	Temp. (°C)	Yield[a] (% of 2)	Yield[a] (% of 3a)	Recovery[a](% of 1) [*E*/*Z*]
1	$PhCH_2$ (**1A**)	None	1.1	−78	0	0	91
2		CuBr/1.1	2.2	−78	0	0	87
3		CuI/1.1	2.2	−78	0	0	76[78/20]
4		CuCN/1.1	2.2	−78	34	0	64[80/20]
5[b,c]		CuCN/1.1	2.2	−78	35	0	52[80/20]
6[c]		CuCN/1.1	2.2	−20	5	0	35[60/40]
7		CuCN/2.2	4.4	−78	66(50)	18	0
8[d]		CuCN/2.2	4.4	−78	56	22	8
9[e]		CuCN/2.2	4.4	−78	63	2	17
10		CuCN/2.2	4.4	−20	0	80(79)	0
11	$PhCH_2CH_2$ (**1B**)	CuCN/2.2	4.4	−78	64(50)	19	0
12	(*Z*)-PhCH=$CHCH_2$ (**1C**)	CuCN/2.2	4.4	−78	55(42)	17	0

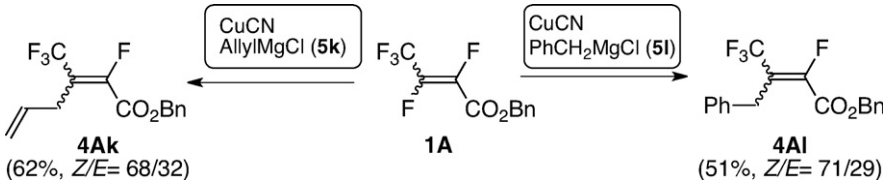
[a] Determined by ^{19}F NMR. Values in parentheses are of isolated yields.
[b] Carried out for 20 h.
[c] Benzyl 4,4,4-trifluoro-2-butynoate was obtained in 4% (for entry 5) and 31% (for entry 6).
[d] Hexamethylphosphoric triamide (HMPA) was used as an additive.
[e] N,N-dimethylformamide (DMF) was used as an additive.

Table 2
Cu(I)-mediated addition–elimination reaction of **1A** with various Grignard reagents .



Entry	Grignard reagent (RMgBr)	Yield[a] (% of **2A**)	Yield[a] (% of **3A**)	Recovery[a] (% of **1A**) [*E*/*Z*]
1	PhMgBr (**5a**)	66 (50)	18	0
2	4-MeOC$_6$H$_4$MgBr (**5b**)	61 (53)	25	Trace
3	3-MeOC$_6$H$_4$MgBr (**5c**)	62 (54)	23	Trace
4	2-MeOC$_6$H$_4$MgBr (**5d**)	23	0	73[90/10]
5	4-MeC$_6$H$_4$MgBr (**5e**)	65 (54)	0	0
6	4-CF$_3$C$_6$H$_4$MgBr (**5f**)	27	0	0
7	*n*-BuMgBr (**5g**)	59 (40)	0	9
8	MeMgBr (**5h**)	60 (38)	0	10
9	*s*-BuMgBr (**5i**)	15	0	79[92/8]
10	PhCH$_2$=CHMgBr (**5j**)	20	0	78[88/12]

[a] Determined by ^{19}F NMR. Values in parentheses are of isolated yields.

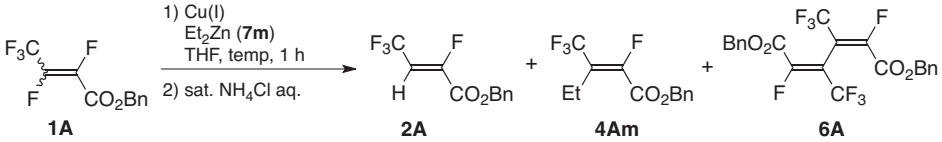


Scheme 3. Cu(I)-mediated addition–elimination reaction of **1A** with allyl- (**5k**) or benzylmagnesium chloride (**5l**).

hydrolysis, resulted in a complex mixture. The use of *n*-butylzinc iodide as an organozinc reagent led to almost quantitative recovery of **1A**. However, it was found that organocuprate, derived from CuBr and diethylzinc (**7m**), was somewhat more reactive, yielding a small amount of the addition–elimination product **4Am** along with 81% recovery of **1A**. Therefore, the reaction of **1A** with diethylzinc (**7m**)-derived organocuprate was investigated in detail, and the results are shown in Table 3.

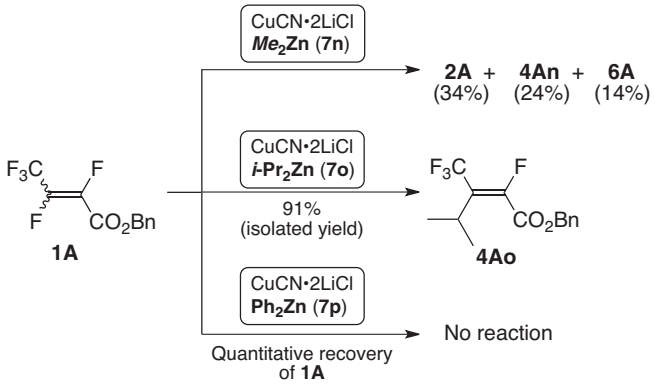
The reaction of benzyl α,β,γ,γ,γ-pentafluorocrotonate (**1A**) with 1.1 equiv. of diethyl zinc (**7m**) in the absence of copper(I) salt in THF at −78 °C for 1 h, followed by addition of an aqueous NH_4Cl solution, did not give any products, a large amount of **1A** being recovered (entry 1). Although various sorts of copper(I) salts, such as CuBr, CuI, and CuCN, were examined, the addition–elimination product **4Am** as well as the reduction product **2A** was not obtained in good yield (entries 2–4). When **1A** was treated with diethyl zinc (**7m**) in the presence of CuCN·2LiCl [14] in THF at −78 °C for 1 h, followed by hydrolysis, the β-reduction product **2A** was produced in 33% yield, along with the addition–elimination product **4Am** and homo-coupling product **6A** [15] in 8% and 10% yields, respectively (entry 5). The use of 2.2 equiv. of organocuprate, prepared from CuCN·2LiCl (2.2 equiv.) and **7m** (4.4 equiv.), resulted in complete consumption of the starting material and improvement on the yield of the β-reduction product **2A** (55%

Table 3
Cu(I)-mediated addition–elimination reaction of **1A** with Et_2Zn .



Entry	Cu(I) salt/equiv.	Equiv. of Et_2Zn	Temp. (°C)	Yield[a] (% of **2A**)	Yield[a] (% of **4Am**)	Yield[a] (% of **6A**)	Recovery[a](% of **1A**) [*E*/*Z*]
1	None	1.1	−78	0	0	0	91 [88/12]
2	CuBr/1.1	2.2	−78	0	11	0	81 [90/10]
3	CuI/1.1	2.2	−78	0	12	0	75 [90/10]
4	CuCN/1.1	2.2	−78	Trace	8	0	83 [90/10]
5	CuCN•2LiCl/1.1	2.2	−78	33	8	10	40 [85/15]
6	CuCN•2LiCl/2.2	4.4	−78	55	7	20	0
7[b]	CuCN•2LiCl/2.2	4.4	−78	54	16	20	0
8[c]	CuCN•2LiCl/2.2	4.4	−78	55	7	14	0
9	CuCN•2LiCl/2.2	4.4	−20	37	20	8	0

[a] Determined by ^{19}F NMR.
[b] With trimethylsilyl chloride (TMSCl) as an additive.
[c] With hexamethylphosphoric triamide (HMPA) as an additive.

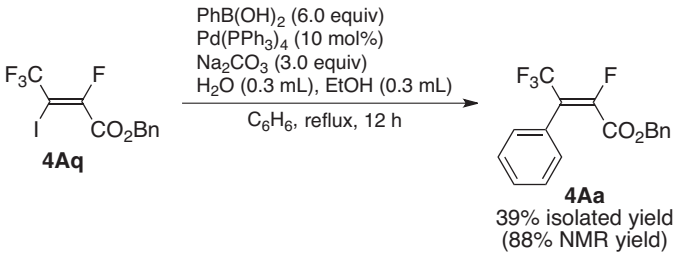


Scheme 4. Cu(I)-mediated addition–elimination reaction of **1A** with Me_2Zn (**7n**), *i*-Pr_2Zn (**7o**) or Ph_2Zn (**7p**).

yield) (entry 6). As shown in entries 7 and 8, the addition of TMSCl or HMPA as an additive [13] did not affect on the yield of **2A** at all. The reaction at higher temperature (−20 °C) led to a complex mixture though the yield of the addition-elimination product **4Am** was slightly increased (entry 9).

In Scheme 4 are shown the results of the reaction of **1A** with some commercially available diorganozinc reagents, such as dimethylzinc (**7n**), diisopropylzinc (**7o**), and diphenylzinc (**7p**), under the conditions shown in entry 6 in Table 3.

The reaction of **1A** with organocuprate derived from CuCN•2LiCl and dimethylzinc (**7n**) yielded three types of products, *i.e.* β-reduction product **2A**, addition–elimination product **4An**, and homo-coupling product **6A**, in 34%, 24%, and 14% yields, respectively. In sharp contrast, diisopropylzinc (**7o**) was quite effective to form the addition–elimination product **4Ao** exclusively as a sole stereoisomer. Diphenylzinc (**7p**) was found to be much less reactive, resulting in quantitative recovery of the starting crotonate **1A**.



Scheme 5. Suzuki–Miyaura cross-coupling reaction of **4Aq** with phenylboronic acid.

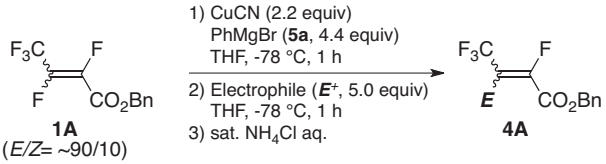
2.3. Cross-coupling reaction leading to fluorine-containing tetra-substituted alkenes

Next we focused our interest on direct cross-coupling reaction of the *in situ*-generated vinylcopper intermediate with various electrophiles, leading to multi-substituted fluorine-containing alkenes. The results are tabulated in Table 4.

Thus, on treating the fluorinated crotonate **1A** with 2.2 equiv. of diphenylcyanocuprate, prepared from CuCN (2.2 equiv.) and phenylmagnesium bromide (**5a**, 4.4 equiv.), in THF at −78 °C for 1 h, followed by addition of I_2 (5.0 equiv.) at the same temperature, benzyl α,γ,γ,γ-tetrafluoro-β-iodocrotonate (**4Aq**) was obtained in 82% (79% isolated) yield as a mixture of the *E*/*Z* isomers (*E*/*Z* = 79/21) (entry 1). Allyl bromide, methallyl bromide, and (*E*)-crotyl bromide as an electrophile could also participate well in the coupling reaction to give the corresponding β-substituted products **4Ak**, **4Ar**, and **4As** in 67% (42% isolated), 66% (62% isolated), and 65% (56% isolated) yields, respectively (entries 2–4). In the case of other electrophiles, like propargyl bromide, benzyl bromide, and trimethylsilyl chloride, only β-reduction product **2A** was observed in 43%, 59%, and 41% yields, respectively.

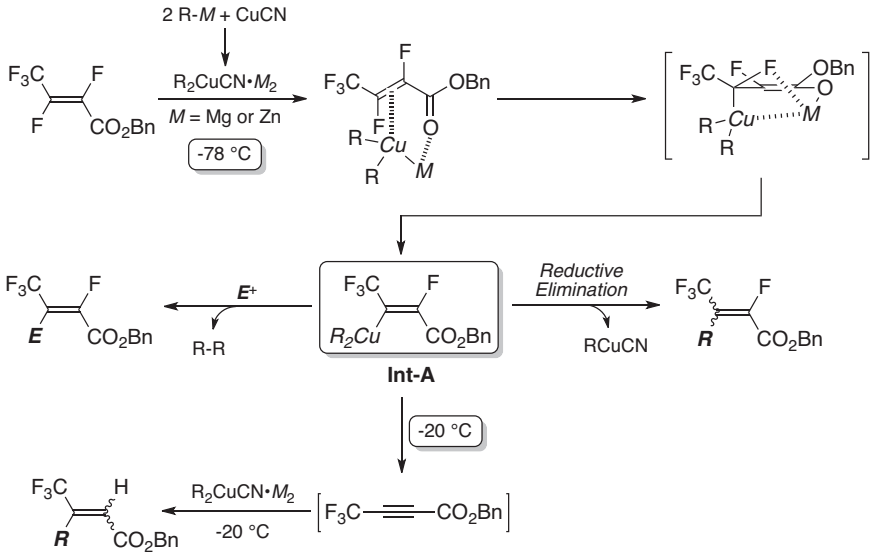
Subsequently, we attempted further transformation of the above-obtained benzyl α,γ,γ,γ-tetrafluoro-β-iodocrotonate

Table 4
Direct cross-coupling reaction with various electrophiles .



Entry	Electrophile	Product	Yield[a] (% of **4A**) [*E*/*Z*]
1	I_2	**4Aq**	82 (79) [79/21]
2	Br	**4Ak**	67 (42) [0/100]
3	Br	**4Ar**	66 (62) [18/82]
4	Br	**4As**	65 (58) [0/100]

[a] Determined by ^{19}F NMR. Values in parentheses are of isolated yields.



Scheme 6. A possible reaction mechanism for the fluorine–copper exchange and subsequent cross-coupling reaction.

(**4Aq**), as shown in Scheme 5. Thus, the reaction of **4Aq** with phenylboronic acid in the presence of 10 mol% of $Pd(PPh_3)_4$, 3.0 equiv. of Na_2CO_3, and 0.3 mL each of H_2O and EtOH in benzene at reflux temperature for 12 h took place efficiently to lead to α,γ,γ,γ-tetrafluoro-β-phenylcrotonate **4Aa** in 88% NMR yield [16].

2.4. Reaction mechanism

A possible mechanism for the fluorine–copper exchange reaction of α,β,γ,γ,γ-pentafluorocrotonates with organocopper reagent and subsequent cross-coupling reaction with electrophiles can be proposed as follows (Scheme 6).

Thus, the *in situ*-generated organocuprate derived from CuCN and organomagnesium or zinc reagent (R-*M*) may coordinate with an olefinic double bond of the fluorinated crotonate, followed by interaction between metal (magnesium or zinc) and the carbonyl oxygen atom, to form a π-complex [17]. Subsequent oxidative addition of the copper species leads to an enolate-like intermediate, which will be in a rigid conformation owing to dual interaction of metal with copper and with fluorine atom [18]. Then, the elimination of metal fluoride takes place to form vinylcopper intermediate **Int-A**, which is stabilized due to the strong electron-withdrawing effect of a CF_3 group [19] and is not susceptible to the reductive elimination at −78 °C [20]. By treatment with various electrophiles, the vinylcopper intermediate **Int-A** is converted to the corresponding β-substituted product, along with the formation of homo-coupling product (R-R). On the other hand, addition–elimination product can be formed with a reductive elimination of RCuCN from **Int-A**, which depends on the nature of substituents on copper center. Although it is still unclear, it is supposed that migratory ability of the substituent from copper center to double bond is one of the most important factors. On raising the reaction temperature from −78 °C to −20 °C, the elimination of *Cu*-F in **Int-A** proceeds to yield the corresponding alkynoate, which may undergo the Michael addition reaction of an excess amount of organocuprate to afford β-substituted γ,γ,γ-trifluorocrotonates as a mixture of the *E*/*Z* isomers.

3. Conclusion

In conclusion, we have found that the fluorine–copper exchange reaction of α,β,γ,γ,γ-pentafluorocrotonate with organomagnesium or zinc-derived organocuprates took place efficiently to generate β-metallated intermediate, of which hydrolysis gave the β-reduction product in good yield. Treatment of the organocopper intermediate with various electrophiles gave the corresponding β-substituted products in good yields. β-Iodinated product was nicely subjected to the Suzuki–Miyaura cross-coupling reaction, leading to the corresponding tetra-substituted fluorinated crotonate in good yield. The present copper–fluorine exchange and subsequent cross-coupling reaction would become a powerful method to prepare various types of organofluorine compounds.

4. Experimental

4.1. General experimental procedures

^1H and ^{13}C NMR spectra were measured with a Bruker DRX-500 (500.13 MHz for ^1H and 125.75 MHz for ^{13}C) spectrometer in a chloroform-*d* ($CDCl_3$) solution with tetramethylsilane as an internal reference. A JEOL JNM-AL400 (376.05 MHz) was used to measure ^{19}F NMR spectra in $CDCl_3$ using trichlorofluoromethane ($CFCl_3$) as an internal standard. Infrared spectra (IR) were determined in a liquid film or KBr disk method with an AVATAR-370DTGS spectrometer (Thermo ELECTRON) or an FT/IR-4100 (JASCO). High resolution mass spectra were taken with a JEOL JMS-700MS spectrometer. Elemental analyses were conducted with a Yanaco CHN CORDER MT-5 instrument.

4.1.1. Materials

All chemicals were of reagent grade, and if necessary, were purified in the usual manner prior to use. Anhydrous tetrahydrofuran (THF) and diethyl ether were purchased from Wako chemicals. Thin layer chromatography (TLC) was done with Merck 25 aluminum sheets (silica gel 60 F_{254}). Column chromatography was carried out with Wakogel C-200. All reactions were carried out under an argon atmosphere.

4.2. General procedure for the preparation of α,β,γ,γ,γ-pentafluorocrotonate

The starting materials, α,β,γ,γ,γ-pentafluorocrotonates **1** were prepared from easily available perfluorobutanoic acid in 3 steps with a slight modification of the reported procedure, as follows: In a two-necked round-bottomed flask, equipped with a stirrer bar, a

rubber septum, and an inlet tube for Ar, was placed 20 mmol of $P(OEt)_3$ [11]. After cooling the flask by immersing in an ice-methanol bath, 10 mmol of freshly prepared perfluorobutanoic acid chloride [11a] was added dropwise to the pre-cooled solution *via* a syringe, followed by continuous stirring at room temperature for 2 h. To the reaction mixture was slowly added 50 mL of water *via* a syringe at 0 °C. The resultant solution was subjected to extraction with Et_2O (50 mL, 3 times) and the ethereal extracts were washed with 5% aqueous $NaHCO_3$ solution, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane/AcOEt = 1/1) to give pure (*Z*)-diethyl 1-(diethylphosphono)-1-perfluorobutenyl phosphate as viscous oil.

4.2.1. (Z)-Diethyl 1-(diethylphosphono)-1-perfluorobutenyl phosphate

Yield: 77% (oil); ^{1}H NMR ($CDCl_3$) δ 1.25 – 1.31 (m, 12H), 4.14 – 4.22 (m, 8H); ^{19}F NMR ($CDCl_3$) δ −137.45 to −137.32 (m, 1F), −119.55 to −119.45 (m, 2F), −84.05 to −83.95 (m, 3F); ^{31}P NMR ($CDCl_3$, H_3PO_4) δ 2.07 (d, J = 10.2 Hz, 1P), −7.22 (dd, J = 10.2, 2.4 Hz, 1P); IR (neat) ν 3412, 2990, 1764, 1481, 1363, 1274, 1216, 1149, 1031, 870 cm^{-1}; HRMS (FAB) calcd for (M + H) $C_{12}H_{21}F_6O_7P_2$: 453.0667, Found: 453.0678.

The vinyl phosphate (5.0 mmol, 2.26 g) prepared was treated with a suspension of CsF (5.5 mmol, 0.84 g) and alcohol (7.5 mmol) in CH_2Cl_2 (10 mL) at 0 °C. After stirring at room temperature for 2 h, the whole was poured into ice-cooled water (30 mL), followed by extraction with Et_2O (30 mL each, 3 times). The organic layers combined were dried over anhydrous Na_2SO_4, filtered and concentrated with a rotary evaporator under reduced pressure. Column chromatography of the residue using hexane/benzene (5/1) gave pure product, α,β,γ,γ,γ-pentafluorocrotonate (**1**) as a mixture of the *E*/*Z* isomers (*E*/*Z* = ∼90/10).

4.2.2. Benzyl α,β,γ,γ,γ-pentafluorocrotonate (*1A*)

Yield: 82% (oil); *E*-**1A**: ^{1}H NMR ($CDCl_3$) δ 5.37 (s, 2H), 7.35 – 7.42 (m, 5H); ^{19}F NMR ($CDCl_3$) δ −153.84 (dq, J = 138.6, 18.8 Hz, 1F), −150.63 (dq, J = 138.6, 6.6 Hz, 1F), −68.91 (dd, J = 18.8, 6.6 Hz, 3F); ^{13}C NMR ($CDCl_3$) δ 68.4, 118.2 (qdd, J = 274.8, 31.4, 4.0 Hz), 128.5, 128.7, 128.9, 134.1, 141.6 (ddq, J = 230.0, 32.8, 2.4 Hz), 145.1 (ddd, J = 273.2, 41.0, 41.0 Hz), 157.3 (dd, J = 30.4, 6.2 Hz); *Z*-**1A**: ^{1}H NMR ($CDCl_3$) δ 5.34 (s, 2H), 7.35 – 7.42 (m, 5H); ^{19}F NMR ($CDCl_3$) δ −136.0 to −137.0 (m, 2F), −65.67 (dd, J = 8.8, 8.8 Hz, 3F); IR (neat) ν 3038, 2966, 1751, 1458, 1372, 1273, 1224, 1162, 960 cm^{-1}; HRMS (EI) Calcd for (M+) $C_{11}H_7F_5O_2$: 266.0366, Found 266.0356; Anal. Calcd for $C_{11}H_7F_5O_2$: C, 49.64: H, 2.65. Found: C, 49.60; H, 2.75.

4.2.3. 2-Phenylethyl α,β,γ,γ,γ-pentafluorocrotonate (*1B*)

Yield: 72% (oil); *E*-**1B**: ^{1}H NMR ($CDCl_3$) δ 3.05 (t, J = 6.9 Hz, 2H), 4.55 (t, J = 6.9 Hz, 2H), 7.23 – 7.30 (m, 3H), 7.31 – 7.37 (m, 2H); ^{19}F NMR ($CDCl_3$) δ −153.70 (dq, J = 139.1, 22.1 Hz, 1F), −151.16 (dq, J = 139.1, 9.8 Hz, 1F), −68.88 (dd, J = 22.1, 9.8 Hz, 3F); ^{13}C NMR ($CDCl_3$) δ 34.7, 67.4, 118.1 (qdd, J = 274.9, 34.9, 3.6 Hz), 126.9, 128.7, 128.9, 136.7, 141.5 (ddq, J = 262.8, 33.1, 2.4 Hz), 145.0 (ddq, J = 273.6, 41.0, 41.0 Hz), 157.4 (dd, J = 30.7, 6.2 Hz); *Z*-**1B**: ^{1}H NMR ($CDCl_3$) δ 3.03 (t, J = 6.5 Hz, 2H), 4.53 (t, J = 6.5 Hz, 2H), 7.23 – 7.30 (m, 3H), 7.31 – 7.37 (m, 2H); ^{19}F NMR ($CDCl_3$) δ −137.1 to −136.7 (m, 1F), −136.4 to −136.1 (m, 1F), −65.67 (dd, J = 9.4, 9.4 Hz, 3F); IR (neat) ν 3031, 2964, 1750, 1702, 1605, 1498, 1375, 1276, 1227, 1163, 984 cm^{-1}; HRMS (FAB) Calcd for (M + H) $C_{12}H_{10}F_5O_2$: 281.0602, Found 281.0594.

4.2.4. 3-Phenyl-2-propen-1-yl α,β,γ,γ,γ-pentafluorocrotonate (*1C*)

Yield: 70% (oil); *E*-**1C**: ^{1}H NMR ($CDCl_3$) δ 5.00 (dd, J = 6.6, 0.8 Hz, 2H), 6.31 (dt, J = 15.8, 6.6 Hz, 1H), 6.76 (d, J = 15.8 Hz, 1H), 7.27 – 7.37 (m, 3H), 7.39 – 7.44 (m, 2H); ^{19}F NMR ($CDCl_3$) δ −153.61 (dq, J = 139.1, 21.8 Hz, 1F), −150.99 (dq, J = 139.1, 9.8 Hz, 1F), −68.88 (dd, J = 21.8, 9.8 Hz, 3F); ^{13}C NMR ($CDCl_3$) δ 67.4, 118.1 (qdd, J = 275.0, 35.3, 3.8 Hz), 120.8, 126.8, 128.5, 128.7, 136.3, 136.6, 141.5 (ddq, J = 230.4, 32.9, 2.4 Hz), 145.1 (ddq, J = 273.7, 40.9, 40.9 Hz), 157.3 (dd, J = 30.2, 6.2 Hz); *Z*-**1C**: ^{1}H NMR ($CDCl_3$) δ 4.98 (dd, J = 6.9, 0.9 Hz, 2H), 6.29 (dt, J = 15.9, 6.9 Hz, 1H), 6.75 (d, J = 15.9 Hz, 1H), 7.27 – 7.37 (m, 3H), 7.39 – 7.44 (m, 2H); ^{19}F NMR ($CDCl_3$) δ −136.8 to −136.5 (m, 1F), −136.4 to −136.1 (m, 1F), −65.65 (dd, J = 9.4, 9.4 Hz, 3F); IR (neat) ν 3029, 2957, 1749, 1701, 1495, 1371, 1270, 1222, 1162, 966 cm^{-1}; HRMS (FAB) Calcd for (M+) $C_{13}H_9F_5O_2$: 292.0523, Found 292.0530.

4.3. Typical procedure for the reaction of *1A* with PhMgBr in the presence of CuCN

A 30 mL two-necked round-bottomed flask, equipped with a magnetic stirrer bar, a rubber septum, and an inlet tube for Ar, was charged with a suspension of CuCN (0.42 mmol, 0.037 g) in THF (1.0 mL). To this solution was slowly added a 1.0 M solution of PhMgBr (0.84 mmol, 0.84 mL) in THF *via* a syringe at −78 °C. The whole was warmed up to −20 °C and stirred for 15 min. To the resulting solution was added benzyl α,β,γ,γ,γ-pentafluorocrotonate (**1A**, 0.19 mmol, 0.050 g) in THF (2.0 mL) *via* a syringe at −78 °C. After being stirred for 1 h, the reaction mixture was poured into an ice-cooled saturated aqueous NH_4Cl solution (30 mL), followed by extraction with Et_2O (30 mL each, 3 times). The organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated with a rotary evaporator. Column chromatography of the residue using hexane/benzene (5/1) yielded pure benzyl (*Z*)-α,γ,γ,γ-tetrafluorocrotonate (**2A**, 0.09 mmol, 0.025 g).

4.3.1. Benzyl (Z)-α,γ,γ,γ-tetrafluorocrotonate (*2A*)

Yield: 50% (oil); ^{1}H NMR ($CDCl_3$) δ 5.33 (s, 2H), 6.28 (dq, J = 28.1, 7.5 Hz, 1H), 7.35 – 7.41 (m, 5H); ^{19}F NMR ($CDCl_3$) δ −111.08 (dq, J = 28.1, 17.3 Hz, 1F), −59.80 (dd, J = 17.3, 7.5 Hz, 3F); ^{13}C NMR ($CDCl_3$) δ 68.6, 106.9, (qd, J = 37.2, 5.6 Hz), 121.1 (q, J = 270.5 Hz), 128.7, 128.8, 129.0, 134.0, 158.5 (d, J = 34.1 Hz), 152.0 (dq, J = 284.4, 5.0 Hz); IR (neat) ν 3038, 2963, 1753, 1697, 1458, 1365, 1283, 1178, 1073, 947 cm^{-1}; HRMS (EI) Calcd for (M+) $C_{11}H_8F_4O_2$: 248.0460, Found 248.0458.

4.3.2. 2-Phenylethyl (Z)-α,γ,γ,γ-tetrafluorocrotonate (*2B*)

Yield: 50% (oil); ^{1}H NMR ($CDCl_3$) δ 3.02 (t, J = 7.0 Hz, 2H), 6.20 (dq, J = 28.1, 7.5 Hz, 1H), 7.20 – 7.37 (m, 5H); ^{19}F NMR ($CDCl_3$) δ −111.24 (dq, J = 28.1, 16.9 Hz, 1F), −59.80 (dd, J = 16.9, 7.5 Hz, 3F); ^{13}C NMR ($CDCl_3$) δ 3.7, 67.3, 106.7 (qd, J = 37.0, 5.6 Hz), 121.1 (q, J = 270.5 Hz), 127.0, 128.7, 128.8, 1136.6, 152.0 (dq, J = 284.8, 4.9 Hz), 158.6 (d, J = 33.9 Hz); IR (neat) ν 3031, 2963, 1753, 1697, 1498, 1396, 1368, 1287, 1183, 1141, 1076, 910 cm^{-1}; HRMS (EI) Calcd for (M+) $C_{12}H_{10}F_4O_2$: 262.0617, Found 262.0608.

4.3.3. (Z)-3-Phenyl-2-propen-1-yl (Z)-α,γ,γ,γ-tetrafluorocrotonate (*2C*)

Yield: 42% (oil); ^{1}H NMR ($CDCl_3$) δ 4.95 (dd, J = 6.8, 1.0 Hz, 2H), 6.30 (dq, J = 28.1, 7.5 Hz, 1H), 6.30 (dt, J = 15.8, 6.8 Hz, 1H), 6.74 (d, J = 15.8 Hz, 1H), 7.25 – 7.38 (m, 3H), 7.39 – 7.43 (m, 2H); ^{19}F NMR ($CDCl_3$) δ −111.17 (dq, J = 28.1, 16.9 Hz, 1F), −59.79 (dd, J = 16.9, 7.5 Hz, 3F); IR (neat) ν 3030, 2957, 1752, 1696, 1496, 1449, 1365, 1276, 1138, 1073, 967 cm^{-1}; HRMS (FAB) Calcd for (M+) $C_{13}H_{10}F_4O_2$: 274.0617, Found 274.0615.

4.3.4. Benzyl γ,γ,γ-trifluorobutynoate

Oil; ^{1}H NMR ($CDCl_3$) δ 5.29 (s, 2H), 7.35 – 7.43 (m, 5H); ^{19}F NMR ($CDCl_3$) δ −52.69 (s, 3F); ^{13}C NMR ($CDCl_3$) δ 69.0, 70.4 (q, J = 54.9 Hz), 75.3 (q, J = 6.5 Hz), 113.3 (q, J = 260.3 Hz), 128.8, 128.81, 129.1, 133.6, 150.6 (q, J = 1.3 Hz); IR (neat) ν 3037, 2965,

1732, 1608, 1457, 1376, 1270, 1163, 1094, 999 cm^{-1}; HRMS (EI) Calcd for (M+) $C_{11}H_7F_3O_2$: 228.0398, Found 228.0393.

4.4. Typical procedure for the preparation of benzyl γ,γ,γ-trifluoro-β-phenylcrotonate (**3Aa**)

A 30 mL two-necked round-bottomed flask equipped with a magnetic stirrer bar, a rubber septum, and an inlet tube for Ar was charged with a suspension of CuCN (0.037 g, 0.42 mmol) in THF (1.0 mL) solution. To the solution was slowly added a 0.84 M solution of PhMgBr (1.0 mL, 0.84 mmol) in THF *via* a syringe at −78 °C. The whole was warmed up to −20 °C and stirred for 15 min. To the resulting solution was added benzyl α,β,γ,γ,γ-pentafluorocrotonate (**1A**, 0.050 g, 0.2 mmol) *via* a syringe at −78 °C. After stirring at −20 °C for 1 h, the reaction mixture was poured into an ice-cooled saturated aqueous NH_4Cl solution (30 mL), followed by extraction with Et_2O (30 mL, 3 times). The organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure with a rotary evaporator. Column chromatography of the residue using hexane/benzene (2/1) yielded pure benzyl γ,γ,γ-trifluoro-β-phenylcrotonate (**3Aa**, 0.046 g, 76%) as an *E*/*Z* mixture.

4.4.1. Benzyl γ,γ,γ-trifluoro-β-phenylcrotonate (**3Aa**)

Yield: 76% (oil); (*E*)-**3Aa**: ^{1}H NMR ($CDCl_3$) δ 5.27 (s, 2H), 6.37 (s, 2H), 7.35 – 7.45 (m, 10H); ^{19}F NMR ($CDCl_3$) δ −60.52 (s, 3F); (*Z*)-**3Aa**: ^{1}H NMR ($CDCl_3$) δ 5.02 (s, 2H), 6.65 (q, *J* = 1.2 Hz, 2H), 7.35 – 7.45 (m, 10H); ^{19}F NMR ($CDCl_3$) δ −68.03 (s, 3F); IR (neat) ν 3065, 3036, 1736, 1656, 1448, 1364, 1284, 1170, 1128, 1003, 949 cm^{-1}; HRMS (FAB) Calcd for (M+H) $C_{17}H_{14}F_3O_2$: 307.0947, Found 307.0951.

4.5. Typical procedure for the reaction of **1A** with $PhCH_2$ MgCl in the presence of CuCN

A 30 mL two-necked round-bottomed flask, equipped with a magnetic stirrer bar, a rubber septum, and an inlet tube for Ar, was charged with a suspension of CuCN (0.42 mmol, 0.037 g) in THF (1.0 mL). To this solution was slowly added a 1.0 *M* solution of $PhCH_2MgCl$ (0.84 mmol, 0.84 mL) in THF *via* a syringe at −78 °C. The whole was warmed up to −20 °C and stirred for 15 min. To the resulting solution was added benzyl α,β,γ,γ,γ-pentafluorocrotonate (**1A**, 0.19 mmol, 0.050 g) in THF (2.0 mL) *via* a syringe at −78 °C. After being stirred for 1 h, the reaction mixture was poured into an ace-cooled saturated aqueous NH_4Cl solution (30 mL), followed by extraction with Et_2O (30 mL each, 3 times). The organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated with a rotary evaporator. Column chromatography of the residue using hexane/benzene (5/1) yielded pure benzyl β-benzyl-α,γ,γ,γ-tetrafluorocrotonate (**4Al**, 0.07 mmol, 0.023 g) as an *E*/*Z* mixture.

4.5.1. Benzyl β-benzyl-α,γ,γ,γ-tetrafluorocrotonate (**4Al**)

Yield: 36% (oil); (*Z*)-**4Al**: ^{1}H NMR ($CDCl_3$) δ 4.03 (s, 2H), 5.32 (s, 2H), 7.15 – 7.40 (m, 10H); ^{19}F NMR ($CDCl_3$) δ −110.33 (q, *J* = 19.5 Hz, 1F), −61.33 (d, *J* = 19.5 Hz, 3F); (*Z*)-**4Al**: ^{1}H NMR ($CDCl_3$) δ 3.70 (d, *J* = 4.0 Hz, 2H), 5.31 (s, 2H), 7.15 – 7.40 (m, 10H); ^{19}F NMR ($CDCl_3$) δ −109.8 to −109.7 (m, 1F), −59.10 (d, *J* = 9.8 Hz, 3F); IR (neat) ν 3066, 2962, 1742, 1686, 1497, 1455, 1347, 1264, 1184, 1077, 996 cm^{-1}; HRMS (FAB) Calcd for (M+Na) $C_{18}H_{14}F_4O_2Na$: 361.0828, Found 361.0822.

4.6. Typical procedure for the preparation of benzyl α,γ,γ,γ-tetrafluoro-β-isopropylcrotonate (**4Ao**)

A 30 mL two-necked round-bottomed flask equipped with a magnetic stirrer bar, a rubber septum, and an inlet tube for Ar was charged with a solution of CuCN (0.037 g, 0.42 mmol) and LiCl (0.035 g, 0.84 mmol) in THF (1.0 mL). To the solution was slowly added a 1.0 M toluene solution of *i*-Pr_2Zn (0.84 mL, 0.84 mmol) at −78 °C. The resulting mixture was stirred at −20 °C for 15 min, and then was re-cooled to −78 °C. To the whole was added dropwise a solution of benzyl α,β,γ,γ,γ-pentafluorocrotonate (**1A**, 0.050 g, 0.2 mmol) in THF (2.0 mL) at −78 °C. After being stirred at −78 °C for 1 h, the reaction mixture was poured into an ice-cooled saturated aqueous NH_4Cl solution (30 mL). The resultant mixture was extracted with Et_2O (30 mL, 3 times) and the organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo* with rotary evaporator. Column chromatography of the residue using hexane/benzene (5/1) gave benzyl (*Z*)-α,γ,γ,γ-tetrafluoro-β-isopropylcrotonate (**4Ao**, 0.050 g, 91%) as a pure product.

4.6.1. Benzyl (*Z*)-α,γ,γ,γ-tetrafluoro-β-isopropylcrotonate (**4Ao**)

Yield: 91% (oil); ^{1}H NMR ($CDCl_3$) δ 1.21 (d, *J* = 7.6 Hz, 6H), 3.65 – 3.80 (m, 1H), 5.30 (s, 2H), 7.33 – 7.45 (m, 5H); ^{19}F NMR ($CDCl_3$) δ −111.47 (q, *J* = 21.8 Hz, 1F), −58.09 (d, *J* = 21.8 Hz, 3F); ^{13}C NMR ($CDCl_3$) δ 20.0, 26.0, 68.0, 123.3 (qd, *J* = 277.7, 2.5 Hz), 127.4 (qd, *J* = 27.3, 3.3 Hz), 128.4, 128.7, 128.8, 134.4, 148.2 (dq, *J* = 279.3, 3.3 Hz), 159.7 (d, *J* = 33.9 Hz); IR (neat) ν 3069, 3037, 2947, 2944, 2885, 1739, 1656, 1457, 1381, 1254, 1139, 1032 cm^{-1}; HRMS (EI) Calcd for (M+) $C_{14}H_{14}F_4O_2$: 290.0930, Found 290.0936.

4.6.2. Benzyl (*Z*)-β-ethyl-α,γ,γ,γ-tetrafluorocrotonate (**4Am**)

NMR Yield: 7% (oil); ^{1}H NMR ($CDCl_3$) δ 1.14 (t, *J* = 7.6 Hz, 3H), 2.63 (q, *J* = 7.6 Hz, 2H), 5.31 (s, 2H), 7.35 – 7.41 (m, 5H); ^{19}F NMR ($CDCl_3$) δ −113.41 (q, *J* = 19.6 Hz, 1F), −62.51 (d, *J* = 19.6 Hz, 3F); IR (neat) ν 3037, 2962, 2875, 1740, 1671, 1456, 1383, 1348, 1246, 1136, 1081 cm^{-1}; HRMS (EI) Calcd for (M+) $C_{13}H_{12}F_4O_2$: 276.0773, Found 276.0785.

4.6.3. Dibenzyl (1*Z*, 3*Z*)-1,4-difluoro-2,3-bis(trifluoromethyl)-1,3-butadiene-1,4-dicarboxylate (**6A**)

NMR Yield: 20% (oil); ^{1}H NMR ($CDCl_3$) δ 5.15 (d, *J* = 11.6 Hz, 2H), 5.27 (d, *J* = 11.6 Hz, 2H), 7.28 – 7.38 (m, 10H); ^{19}F NMR ($CDCl_3$) δ −101.45 (q, *J* = 17.3 Hz, 2F), −61.07 (d, *J* = 17.3 Hz, 6F); ^{13}C NMR ($CDCl_3$) δ 69.0, 111.4 – 112.9 (m), 120.6 (qd, *J* = 276.8, 4.2 Hz), 128.8, 128.9, 129.2, 133.5, 151.6 (dq, *J* = 289.3, 2.5 Hz), 157.6 (d, *J* = 33.0 Hz); IR (neat) ν 3037, 2964, 1750, 1655, 1458, 1333, 1261, 1215, 1160, 954 cm^{-1}; HRMS (FAB) Calcd for (M+H) $C_{22}H_{15}F_8O_4$: 495.0843, Found 495.0815.

4.7. Typical procedure for the preparation of benzyl α,γ,γ,γ-tetrafluoro-β-iodocrotonate (**4Aq**)

A 30 mL two-necked round-bottomed flask, equipped with a magnetic stirrer bar, a rubber septum, and an inlet tube for Ar, was charged with a suspension of CuCN (0.037 g, 0.42 mmol) in THF (1.0 mL). To the solution was slowly added a 0.84 M solution of PhMgBr (1.0 mL, 0.84 mmol) in THF *via* a syringe at −78 °C. The whole was warmed up to −20 °C and stirred for 15 min. To the resulting solution was added dropwise benzyl α,β,γ,γ,γ-pentafluorocrotonate (**1A**, 0.050 g, 0.2 mmol) in THF (2.0 mL) *via* a syringe at −78 °C. After being stirred at the same temperature for 1 h, the mixture was treated with iodine (0.241 g, 0.95 mmol) in THF (2.0 mL) at −78 °C. After stirring at −78 °C for 1 h, the reaction mixture was poured into an ice-cooled saturated aqueous NH_4Cl solution (30 mL), followed by extraction with Et_2O (30 mL, 3 times). The organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure with rotary evaporator. Column chromatography of the residue using hexane/benzene (2/1) yielded pure benzyl α,γ,γ,γ-tetrafluoro-β-iodocrotonate (**4Aq**, 0.058 g, 79%) as a sole product.

*4.7.1. Benzyl (E)-α,γ,γ,γ-tetrafluoro-β-iodocrotonate (**4Aq**)*

Yield: 79% (oil); ^{1}H NMR ($CDCl_3$) δ 5.35 (s, 2H), 7.35 – 7.50 (m, 5H); ^{19}F NMR ($CDCl_3$) δ −80.78 (q, J = 24.4 Hz, 1F), −58.25 (d, J = 24.4 Hz, 3F); ^{13}C NMR ($CDCl_3$) δ 68.8, 74.0 (qd, J = 30.7, 11.6 Hz), 120.9 (q, J = 274.9 Hz), 128.7, 128.7, 129.0, 133.9, 150.9 (dq, J = 294.1, 2.8 Hz), 158.5 (d, J = 33.6 Hz); IR (neat) ν 3069, 2962, 1743, 1627, 1498, 1312, 1237, 1187, 1147, 956 cm^{-1}; HRMS (FAB) Calcd for (M+) $C_{11}H_7F_4IO_2$: 373.9427, Found 373.9438; Anal. Calcd for $C_{11}H_7F_4IO_2$: C, 35.32: H, 1.89, Found: C, 35.50: H, 1.92.

*4.7.2. Benzyl (Z)-β-allyl-α,γ,γ,γ-tetrafluorocrotonate (**4Ak**)*

Yield: 42% (oil); ^{1}H NMR ($CDCl_3$) δ 3.39 (dd, J = 2.5, 1.5 Hz, 2H), 5.12 (dd, J = 10.0, 1.5 Hz, 1H), 5.14 (dd, J = 16.5, 1.5 Hz, 1H), 5.31 (s, 2H), 5.78 (dq, J = 16.5, 10.0 Hz, 1H), 7.34 – 7.44 (m, 5H); ^{19}F NMR ($CDCl_3$) δ −111.38 (q, J = 19.6 Hz, 1F), −62.10 (d, J = 19.6 Hz, 3F); ^{13}C NMR ($CDCl_3$) δ 29.2 (q, J = 1.6 Hz), 68.1, 117.9, 121.4 (qd, J = 30.5, 5.8 Hz), 122.6 (q, J = 260.2 Hz), 128.5, 128.7, 128.9, 132.2 (d, J = 3.6 Hz), 134.3, 148.9 (dq, J = 281.4, 3.8 Hz), 159.3 (d, J = 32.9 Hz); IR (neat) ν 3070, 2961, 1739, 1672, 1499, 1348, 1274, 1186, 1143, 1097, 968 cm^{-1}; HRMS (EI) Calcd for (M+) $C_{14}H_{12}F_4O_2$: 288.0773, Found 288.0760.

*4.7.3. Benzyl (Z)-α,γ,γ,γ-tetrafluoro-β-methayllylcrotonate (**4Ar**)*

Yield: 62% (oil); ^{1}H NMR ($CDCl_3$) δ 1.73 (s, 3H), 3.35 (brs, 2H), 4.71 (brs, 1H), 4.86 (brs, 1H), 5.30 (s, 2H), 7.25 – 7.45 (m, 5H); ^{19}F NMR ($CDCl_3$) δ −110.29 (q, J = 19.5 Hz, 1F), −62.25 (d, J = 19.5 Hz, 3F); ^{13}C NMR ($CDCl_3$) δ 22.5, 32.6 (q, J = 3.8 Hz), 68.1, 112.1, 121.4 (qd, J = 29.6, 5.7 Hz), 122.5 (q, J = 276.8 Hz), 128.5, 128.7, 128.8, 134.2, 130.4 (d, J = 3.5 Hz), 149.5 (dq, J = 279.4, 2.8 Hz), 159.3 (d, J = 33.9 Hz); IR (neat) ν 3037, 2975, 1740, 1670, 1456, 1347, 1277, 1220, 1143, 1120, 969 cm^{-1}; HRMS (EI) Calcd for (M+) $C_{15}H_{14}F_4O_2$: 302.0930, Found 302.0920.

*4.7.4. Benzyl (Z)-β-crotyl-α,γ,γ,γ-tetrafluorocrotonate (**4As**)*

Yield: 58% (oil); ^{1}H NMR ($CDCl_3$) δ 1.65 (d, J = 6.4 Hz, 3H), 3.31 (d, J = 6.2 Hz, 2H), 5.31 (s, 2H), 5.37 (dt, J = 16.0, 6.2 Hz, 1H), 5.56 (dq, J = 16.0, 6.2 Hz, 1H), 7.35 – 7.45 (m, 5H); ^{19}F NMR ($CDCl_3$) δ −112.42 (q, J = 18.8 Hz, 1F), −61.99 (d, J = 18.8 Hz, 3F); ^{13}C NMR ($CDCl_3$) δ 17.8, 28.1 (q, J = 9.4 Hz), 68.0, 122.2 (qd, J = 29.6 Hz, 4.9 Hz), 122.7 (q, J = 274.9 Hz), 124.6 (d, J = 3.6 Hz), 128.5, 128.7, 128.8, 129.0, 134.3, 148.4 (dq, J = 272.1 Hz, 3.6 Hz), 159.4 (d, J = 33.9 Hz); IR (neat) ν 3035, 2965, 1740, 1672, 1456, 1348, 1266, 1210, 1143, 1122, 1099, 967 cm^{-1}; HRMS (EI) Calcd for (M+) $C_{15}H_{14}F_4O_2$: 302.0930, Found 302.0935.

4.8. Typical procedure for Pd(0)-catalyzed Suzuki–Miyaura cross-coupling of (E)-4Aq with PhB(OH)$_2$

A 30 mL two-necked round-bottomed flask, equipped with a magnetic stirrer bar, a rubber septum, and an inlet tube for Ar, was charged with a suspension of 10 mol% of $Pd(PPh_3)_4$ and benzyl (*E*)-α,γ,γ,γ-tetrafluoro-β-iodocrotonate (**4Aq**, 0.050 g, 0.13 mmol) in benzene (3.0 mL). To the suspension were added Na_2CO_3 (0.042 g, 0.40 mmol), $PhB(OH)_2$ (0.097 g, 0.80 mmol), 0.30 mL each of H_2O and EtOH, and the whole was stirred at reflux temperature for 12 h. The reaction mixture was poured into an ice-cooled saturated aqueous NH_4Cl solution (30 mL), followed by extraction with Et_2O (30 mL, 3 times each). The organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. Column chromatography of the residue using hexane/benzene (2/1) yielded pure benzyl (*Z*)-α,γ,γ,γ-tetrafluoro-β-phenylcrotonate (**4Aa**, 0.016 g, 39%) as a pure compound.

*4.8.1. Benzyl (Z)-α,γ,γ,γ-tetrafluoro-β-phenylcrotonate (**4Aa**)*

Yield: 39% (oil); ^{1}H NMR ($CDCl_3$) δ 5.03 (s, 2H), 7.30 – 7.45 (m, 10H); ^{19}F NMR ($CDCl_3$) δ −108.66 (q, J = 24.4 Hz, 1F), −60.98 (d, J = 24.4 Hz, 3F); IR (neat) ν 3035, 2960, 1736, 1498, 1364, 1284, 1260, 1172, 1133, 1004 cm^{-1}; HRMS (FAB) Calcd for (M+) $C_{17}H_{12}F_4O_2$: 324.0773, Found 324.0777.

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