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Journal of Fluorine Chemistry 127 (2006) 966–972
JOURNAL OF FLUORINE CHEMISTRY
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Highly stereoselective one-pot synthesis of tetrasubstituted alkenes via carbopalladation reaction of fluorine-containing acetylene derivatives

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Received 22 March 2006; received in revised form 27 April 2006; accepted 27 April 2006
Available online 2 May 2006

Abstract

Treatment of fluoroalkylated alkynes with various aryl halides and arylboronic acids in the presence of Pd(0) in DMF/H_2O at 100 °C for 2 h led to the smooth three-component coupling reaction, the corresponding tetrasubstituted alkenes being obtained in high yields stereoselectively.

Keywords: A fluoroalkyl group; Carbopalladation; One-pot reaction; Tetrasubstituted alkenes; Fluorine-containing alkynes

1. Introduction

Partially fluorinated organic molecules often possess properties that make them suitable for diverse applications in the area of materials science, agrochemistry, and pharmaceutical industry [1]. Consequently, much attention has been focused on the development of the efficient and practical synthetic methods for the preparation of such molecules [2].

Among various types of fluorinated compounds, tetrasubstituted alkenes **1** possessing a fluoroalkyl group, shown in Fig. 1, are recognized as one of the most important synthetic targets because of their physically as well as chemically unique properties [3]. Although several synthetic approaches to the fluoroalkylated alkenes have been reported thus far, they sometimes suffer from multi-step manipulations, low stereoselectivities, harsh reaction conditions, etc [4].

Recently, we have developed highly regio- and stereoselective hydrostannation [5], hydroboration [6], carbocupration [7], and carbostannylation reactions [8] of fluoroalkylated acetylene derivatives **2**, which realized the efficient as well as practical approaches to **1** [9]. Herein we wish to describe the practical one-step coupling reaction of three components, such as aryl iodides, fluoroalkylated alkynes, and arylboronic acids, leading to the corresponding tetrasubstituted alkenes stereoselectively.

2. Results and discussion

2.1. One-pot synthesis of fluorine-containing tetrasubstituted alkenes

Initially, the reaction of trifluoromethylated internal alkyne **2a** [10] with iodobenzene and phenylboronic acid in the presence of palladium catalyst was examined (Table 1) [11]. Thus, treatment of **2a** with 2.0 equiv. of PhI and 3.0 equiv. of $PhB(OH)_2$ in DMF/H_2O in the presence of 10 mol% of $PdCl_2(PhCN)_2$ and 3.0 equiv. of K_2CO_3 at 100 °C for 2 h gave the corresponding tetrasubstituted alkene **1a** in 73% yield as a sole product (Entry 1). In this case, neither stereoisomer **3** nor the Suzuki-Miyaura cross-coupling product **4** was detected at all (Fig. 2). Reducing the amount of the catalyst from 10 mol% to 5 mol% led to an increase of the yield as shown in Entry 2. Additionally, the reaction with 2.0 equiv. each of PhI and $PhB(OH)_2$ gave **1a** in 93% yield (Entry 3). The use of 1.2 equiv. of PhI, on the other hand, resulted in an appreciable decrease of the yield (Entry 4).

With this optimized reaction conditions, we next examined the reaction with various fluoroalkylated alkynes, aryl iodides and arylboronic acids as summarized in Table 2.

As shown in Entries 1–3, various aryl halides or arylboronic acids, such as *p*-methoxyphenyl, *p*-methylphenyl iodides or

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0022-1139/$ – see front matter
doi:10.1016/j.jfluchem.2006.04.012

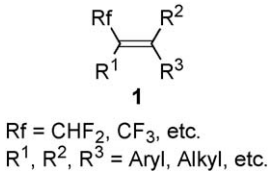
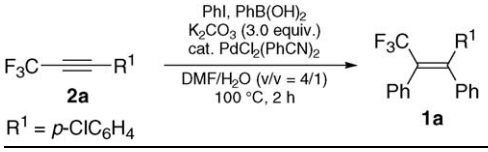


Fig. 1. Fluoroalkylated tetrasubstituted alkenes.

Table 1
Investigation of the reaction conditions for three-component coupling



Entry	PhI/equiv.	$PhB(OH)_2$/equiv.	Pd/mol%	Yield[a]/%
1	2.0	3.0	10	73
2	2.0	3.0	5	84
3	2.0	2.0	5	93 (85)
4	1.2	2.0	5	80

[a] Determined by ^{19}F NMR. Value in parentheses is of isolated yield.

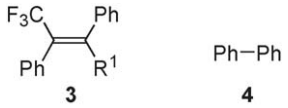
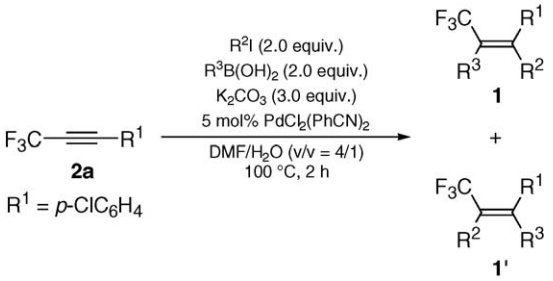


Fig. 2. A stereoisomer **3** and biphenyl (**4**).

boronic acids could participate nicely in the coupling reaction to give the corresponding tetrasubstituted alkenes in high yields. Various substituents on the benzene ring of **2**, such as a chloro, methoxy, methyl and ethoxycarbonyl group, did not influence the reaction at all (Entries 1, 4–6). Additionally, the alkynes having an *ortho*-or *meta*-substituted aromatic ring as R^1 were also applied for the coupling reaction successfully

Table 3
Examination of the regioselectivity



Entry	R^2	R^3	Yield[a] of (**1** + **1′**)/%	Ratio (**1**:**1′**)[a]
1	Ph	p-$MeOC_6H_4$	76 (**A**)	40:60
2	p-$MeOC_6H_4$	Ph	80	63: 37[b]
3	p-MeC_6H_4	Ph	89 (**B**)	39:61
4	p-$EtO_2CC_6H_4$	Ph	76 (**C**)	71:29
5	m-$MeOC_6H_4$	Ph	84 (**D**)	57:43
6	o-$MeOC_6H_4$	Ph	60 (**E**)	62:38

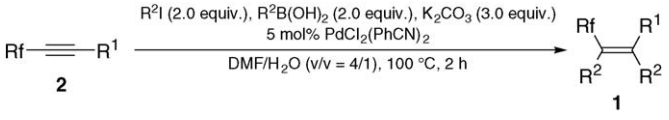
[a] Determined by ^{19}F NMR.
[b] Ratio = **1A**:**1′A**.

(Entries 4, 7, 8). The alkyne having an alkyl group as R^1 was also found to be effective for the reaction (Entry 9), though the benzyl group as R^1 did not give any desired product (Entry 10). Switching a fluoroalkyl group from a trifluoromethyl to a difluoromethyl or hexafluoropropyl group did not cause any significant change for the reaction (Entries 11 and 12).

We next examined the regioselectivity in this three-component coupling reaction as described in Table 3.

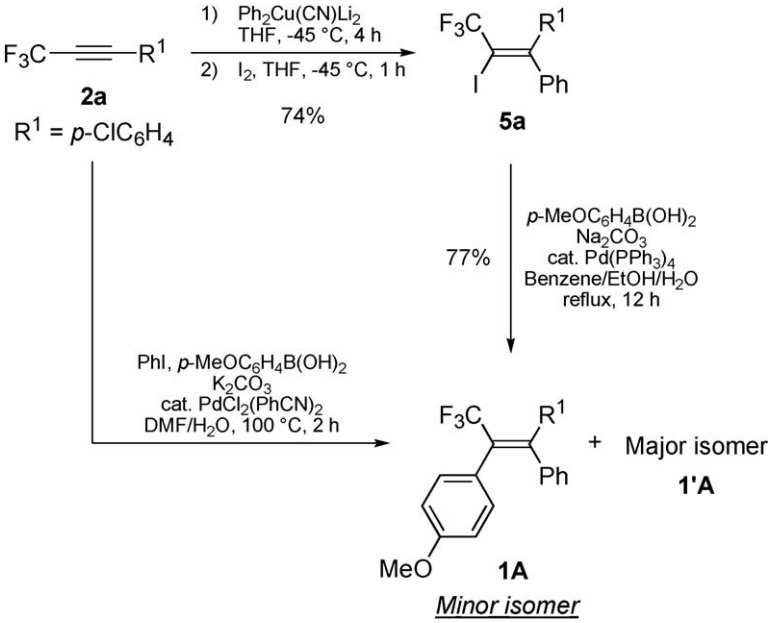
Even when R^2 and R^3 were different, the reaction proceeded smoothly in a highly *cis*-selective manner, giving the corresponding tetrasubstituted alkenes **1** and **1′** in high yields. However, the regioselectivity was found to be substantially low. Changing R^2 from an electron-donating group to an electron-withdrawing group did not lead to a high regioselectivity (Entry 4). Additionally, no influence of the position of the substituent

Table 2
Three-component coupling reaction using various fluoroalkylated alkynes



Entry	Rf	R^1	Substrate	R^2	Product	Yield[a]/%
1	CF_3	p-ClC_6H_4	**2a**	Ph	**1a**	93 (85)
2	CF_3	p-ClC_6H_4	**2a**	p-$MeOC_6H_4$	**1b**	86
3	CF_3	p-ClC_6H_4	**2a**	p-MeC_6H_4	**1c**	85 (82)
4	CF_3	p-$MeOC_6H_4$	**2b**	Ph	**1d**	88
5	CF_3	p-MeC_6H_4	**2c**	Ph	**1e**	85 (81)
6	CF_3	p-$EtO_2CC_6H_4$	**2d**	Ph	**1f**	69
7	CF_3	m-$MeOC_6H_4$	**2e**	Ph	**1g**	87(71)
8	CF_3	o-$MeOC_6H_4$	**2f**	Ph	**1h**	85
9	CF_3	$Ph(CH_2)_3$	**2g**	Ph	**1i**	83
10	CF_3	p-$MeOC_6H_4CH_2$	**2h**	Ph	-	0
11	CHF_2	p-ClC_6H_4	**2i**	Ph	**1j**	81 (80)
12	$CHF_2CF_2CF_2$	p-$C1C_6H_4$	**2j**	Ph	**1k**	87 (73)

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

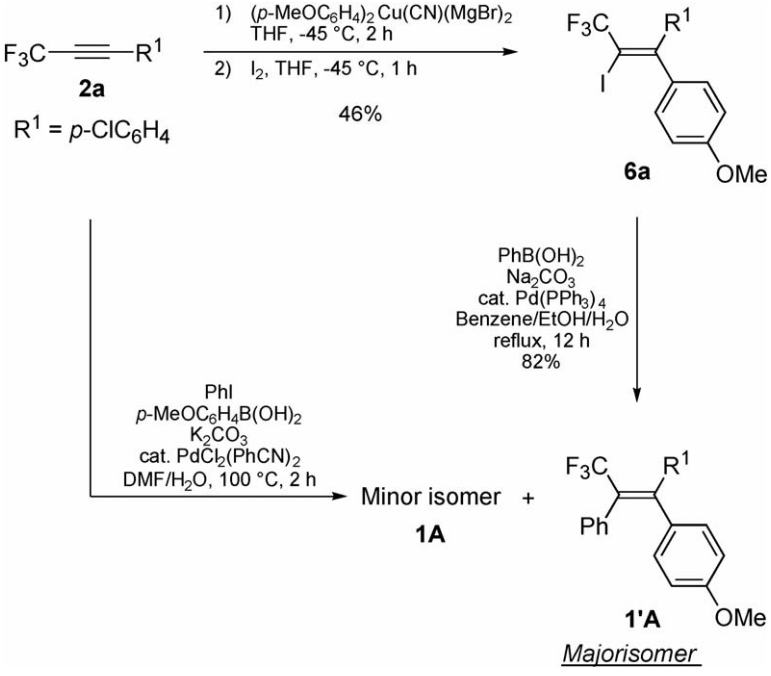


Scheme 1. Stereochemical assignment of **1A**.

on R^2 was observed (Entries 5 and 6). In order to improve the regioselectivity, we examined various types of catalysts, such as $PdCl_2(PPh_3)_2$, $Pd(OAc)_2$, $Pd_2(dba)_3 + P(o\text{-Tol})_3$, $Pd_2(dba)_3 + P(c\text{-Hex})_3$, $Pd_2(dba)_3$ + dppe, and so on. All reactions took place smoothly to give the corresponding tetrasubstituted alkenes in good to high yields but with low regioselectivity (ca. 60:40). On the other hand, the use of other metal catalyst, such as $Ni(COD)_2$, $RhCl(PPh_3)_3$, and $Rh(COD)_2BF_4$ did not give the desired compounds at all.

2.2. Stereochemistry

The stereochemical outcome of the reactions in Table 3 was determined as follows. Thus, treatment of **2a** with $Ph_2Cu(CN)Li_2$ in THF at −45 °C for 4 h followed by the addition of an excess amount of I_2 gave the corresponding vinyl iodide **5a** (Scheme 1). The subsequent Suzuki-Miyaura cross-coupling reaction of **5a** proceeded smoothly to afford the corresponding tetrasubstituted alkene. This alkene was found to be totally identical to the minor



Scheme 2. Stereochemical assignment of **1′A**.

isomer **1A** in the three-component coupling reaction of **2a** with PhI and (p-$MeOC_6H_4$)$B(OH)_2$, on the basis of ^1H and ^{19}F NMR analysis. On the other hand, the reaction of **2a** with (p-$MeOC_6H_4$)$_2Cu(CN)(MgBr)_2$ in THF at −45 °C for 2 h followed by the addition of an excess amount of I_2 afforded the vinyl iodide **6a** (Scheme 2). The following Suzuki-Miyaura cross-coupling reaction gave the corresponding tetrasubstituted alkene in 82% yield. ^1H and ^{19}F NMR analyses showed that the alkene derived from **2a** via carbocupration was totally identical to the **1′A**. The stereochemical assignments of the other products were determined with the comparison of the chemical shift in ^{19}F NMR.

3. Conclusion

In summary, we have developed the practical one-pot method for the preparation of fluoroalkylated tetrasubstituted alkenes, starting from a variety of fluoroalkylated alkynes. Various types of alkynes were demonstrated to be suitable for the present reaction, affording the desired compounds in high yields. In all cases, a complete stereoselectivity was observed.

4. Experimental

4.1. General experimental procedures

^1H NMR spectra were measured with a Bruker DRX (500.13 MHz) spectrometer in a chloroform-d ($CDCl_3$) solution with tetramethylsilane (Me_4Si) as an internal reference. ^{13}C NMR spectra were recorded on a Bruker DRX (125.77 MHz). A JEOL JNM-EX90F (84.21 MHz, FT) spectrometer was used for determining ^{19}F NMR yield with internal C_6F_6. It was also used for determining regioselectivity and stereoselectivity and for taking ^{19}F NMR spectra in a $CDCl_3$ solution with internal $CFCl_3$. $CFCl_3$ was used ($\delta_F = 0$) as an internal standard for ^{19}F NMR. Infrared spectra (IR) were recorded on a Shimadzu FTIR-8200A (PC) spectrophotometer. Mass spectra (MS) were taken on a JEOL JMS-700.

4.2. Materials

Tetrahydrofuran (THF) and copper cyanide were commercially available from Wako chemicals Co. All chemicals were of reagent grade and, if necessary, were purified in the usual manner prior to use. Thin layer chromatography (TLC) was done with Merck silica gel 60 F_{254} plates and column chromatography was carried out with Wako gel C-200. All acetylenes were prepared according to the previous literature procedure [10].

4.3. Typical procedure for the Palladium-catalyzed reaction of fluoroalkylated acetylene derivatives with arylboronic acid and aryl iodide

To a solution of K_2CO_3 (104 mg, 0.75 mmol), PhI (102 mg, 0.50 mmol), $PhB(OH)_2$ (61 mg, 0.50 mmol) and $PdCl_2(PhCN)_2$ (5 mg, 0.05 mmol) in DMF (2 mL)/H_2O (1 mL) was added a solution of 1-(4-chlorophenyl)-3,3,3-trifluoropropyne (51 mg, 0.25 mmol) in DMF (2 mL) at room temperature. The whole was heated at 100 °C for 2 h, and allowed to cool to room temperature. The reaction mixture was poured into sat. NH_4Cl aq. and the whole was extracted with ether three times. The combined organic layers were washed with sat. NaCl aq., dried over anhydrous Na_2SO_4, and then concentrated in vacuo. The residue was purified by silica gel column chromatography to give the corresponding (*Z*)-1-(4-chlorophenyl)-1,2-diphenyl-3,3,3-trifluoropropene (**1a**) (83 mg, 0.21 mmol, 85% yield).

4.3.1. (Z)-1-(4-Chlorophenyl)-1,2-diphenyl-3,3,3-trifluoropropene (*1a*)

Yield: 85%; M.P. 92–94 °C; ^1H NMR ($CDCl_3$) δ = 6.87–6.89 (m, 2H), 7.04–7.05 (m, 3H), 7.19–7.25 (m, 7H), 7.34 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 123.5 (q, J = 275.5 Hz), 127.6, 127.8, 128.0, 128.3, 129.6, 129.93, 129.94, 130.1 (q, J = 28.9 Hz), 131.3, 134.0, 134.7, 138.9, 140.5, 149.1 (q, J = 3.4 Hz); ^{19}F NMR ($CDCl_3$) δ = –55.8 (s, 3F); IR (KBr) 1606, 1490, 1444, 1326, 1309 cm^{-1}; HRMS calcd. for $C_{21}H_{14}ClF_3$ (M^+) 358.0736; found, 358.0743.

4.3.2. (Z)-1-(4-Chlorophenyl)-1,2-bis(4-methoxyphenyl)-3,3,3-trifluoropropene (1b)

Yield: 86% (Determined by ^{19}F NMR); M.P. 99–101 °C; ^1H NMR ($CDCl_3$) δ = 3.69 (s, 3H), 3.76 (s, 3H), 6.58 (d, J = 8.8 Hz, 2H), 6.76 (d, J = 8.8 Hz, 2H), 6.79 (d, J = 8.8 Hz, 2H), 7.15 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 55.05, 55.12, 113.2, 113.6, 123.7 (q, J = 275.3 Hz), 127.3, 128.2, 128.5 (q, J = 28.7 Hz), 130.2, 131.5, 132.7, 133.0, 133.8, 139.5, 148.1 (q, J = 3.4 Hz), 158.8, 159.1; ^{19}F NMR ($CDCl_3$) δ = –56.1 (s, 3F); IR (KBr) 2835, 1606, 1571, 1510, 1461 cm^{-1}; HRMS calcd. for $C_{23}H_{18}ClF_3O_2$ (M^+) 418.0947; found, 418.0947.

4.3.3. (Z)-1-(4-Chlorophenyl)-1,2-bis(4-methylphenyl)-3,3,3-trifluoropropene (1c)

Yield: 82%; ^1H NMR ($CDCl_3$) δ = 2.20 (s, 3H), 2.30 (s, 3H), 6.79 (d, J = 8.0 Hz, 2H), 6.87 (d, J = 7.9 Hz, 2H), 7.04 (d, J = 7.9 Hz, 2H), 7.14 (d, J = 7.8 Hz, 2H), 7.24 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 55.05, 55.12, 113.15, 113.56, 123.72 (q, J = 275.3 Hz), 127.32, 128.18, 128.51 (q, J = 28.7 Hz), 130.15, 131.46, 132.66, 133.01, 133.78, 139.46, 148.14 (q, J = 3.4 Hz), 158.76, 159.10; ^{19}F NMR ($CDCl_3$) δ = −56.12 (s, 3F); IR (neat) 3028, 2922, 2868, 1905, 1610, 1593 cm^{-1}; HRMS calcd. for $C_{23}H_{18}ClF_3$ (M^+) 386.1049; found, 386.1048.

4.3.4. (Z)-1-(4-Methoxyphenyl)-1,2-diphenyl-3,3,3-trifluoropropene (*1d*)

Yield: 88% (Determined by ^{19}F NMR); ^1H NMR ($CDCl_3$) δ = 3.83 (s, 3H), 6.88–6.92 (m, 4H), 7.03–7.04 (m, 3H), 7.18–7.30 (m, 7H); ^{13}C NMR ($CDCl_3$) δ = 55.2, 113.4, 123.7 (q, J = 275.1 Hz), 127.3, 127.6, 127.7, 127.8, 128.8 (q, J = 28.5 Hz), 129.8, 130.0, 131.5, 132.8, 135.3, 141.4, 150.2 (q, J = 3.0 Hz), 159.3; ^{19}F NMR ($CDCl_3$) δ = −56.2 (s, 3F); IR (KBr) 3003, 2908, 2837, 1608, 1573, 1510 cm^{-1}; HRMS calcd. for $C_{22}H_{17}F_3O$ (M^+) 354.1232; found, 354.1228.

*4.3.5. (Z)-1-(4-Methylphenyl)-1,2-diphenyl-3,3,3-trifluoropropene (**1e**)*

Yield: 81%; M.P. 118–120 °C; ^{1}H NMR ($CDCl_3$) δ = 2.37 (s, 3H), 6.90–6.92 (m, 2H), 7.02–7.04 (m, 3H); ^{13}C NMR ($CDCl_3$) δ = 21.3, 123.5 (q, J = 275.6 Hz), 127.2, 127.6, 127.7, 127.9, 128.5, 128.7, 129.1 (q, J = 28.7 Hz), 129.7, 131.5, 135.1, 137.6, 137.7, 141.2, 150.5 (q, J = 3.2 Hz); ^{19}F NMR ($CDCl_3$) δ = −56.2 (s, 3F); IR (KBr) 3082, 3020, 2914, 2866, 1606 cm^{-1}; HRMS calcd. for $C_{22}H_{17}F_3$ (M^+) 338.1282; found, 338.1284.

*4.3.6. Ethyl 4-((Z)-1,2-diphenyl-3,3,3-trifluoropropenyl)benzoate (**1f**)*

Yield: 69% (Determined by ^{19}F NMR); M.P. 93–95 °C; ^{1}H NMR ($CDCl_3$) δ = 1.40 (t, J = 7.1 Hz, 3H), 4.39 (q, J = 7.1 Hz, 2H), 6.89–6.90 (m, 2H), 7.04–7.05 (m, 3H), 7.21–7.23 (m, 5H), 7.39 (d, J = 8.2 Hz, 2H), 8.05 (d, J = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.3, 61.1, 123.4 (q, J = 275.7 Hz), 127.6, 127.8, 128.00, 128.03, 128.5, 129.3, 129.6, 129.9, 130.1 (q, J = 29.4 Hz), 131.2, 134.5, 140.1, 145.0, 149.2 (q, J = 3.4 Hz), 166.2; ^{19}F NMR ($CDCl_3$) δ = −56.2 (s, 3F); IR (KBr) 2981, 1714, 1606, 1490, 1463 cm^{-1}; HRMS calcd. for $C_{24}H_{19}F_3O_2$ (M^+) 396.1337; found, 396.1330.

*4.3.7. (Z)-1-(3-Methoxyphenyl)-1,2-diphenyl-3,3,3-trifluoropropene (**1g**)*

Yield: 71%; M.P. 91–93 °C; ^{1}H NMR ($CDCl_3$) δ = 3.81 (s, 3H), 6.87–6.96 (m, 5H), 7.04–7.05 (m, 3H), 7.20–7.26 (m, 5H), 7.29 (t, J = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ = 55.2, 113.2, 114.3, 121.0, 123.6 (q, J = 275.3 Hz), 127.3, 127.7, 127.8, 127.9, 129.0, 129.4 (q, J = 29.7 Hz), 129.5, 131.4, 134.9, 140.7, 141.7, 150.1 (q, J = 3.4 Hz), 159.2; ^{19}F NMR ($CDCl_3$) δ = −56.4 (s, 3F); IR (KBr) 1575, 1487, 1458, 1446, 1429 cm^{-1}; HRMS calcd. for $C_{22}H_{18}F_3O$ (M + H) 355.1310; found, 355.1315.

*4.3.8. (Z)-1-(2-Methoxyphenyl)-1,2-diphenyl-3,3,3-trifluoropropene (**1h**)*

Yield: 85% (Determined by ^{19}F NMR); M.P. 91–93 °C; ^{1}H NMR ($CDCl_3$) δ = 3.75 (s, 3H), 6.90 (d, J = 8.3 Hz, 1H), 6.95–6.97 (m, 1H), 6.98–7.32 (m, 12H); ^{13}C NMR ($CDCl_3$) δ = 55.6, 111.1, 120.2, 123.6 (q, J = 275.2 Hz), 127.0, 127.4, 127.7, 127.8, 129.2, 129.3, 129.4, 129.76, 130.3 (q, J = 28.7 Hz), 131.3, 134.9, 140.5, 146.1 (q, J = 3.5 Hz), 156.1; ^{19}F NMR ($CDCl_3$) δ = −58.8 (s, 3F); IR (KBr) 3003, 2837, 1596, 1583, 1490 cm^{-1}; HRMS calcd. for $C_{22}H_{17}F_3O$ (M^+) 354.1232; found, 354.1223.

*4.3.9. (Z)-2,3,6-Triphenyl-1,1,1-trifluoro-2-hexene (**1i**)*

Yield: 83% (Determined by ^{19}F NMR); ^{1}H NMR ($CDCl_3$) δ = 1.64 (m, 2H), 2.62 (t, J = 7.9 Hz, 2H), 2.78–2.82 (m, 2H), 6.89–6.91 (m, 2H), 6.97–6.99 (m, 2H), 7.05–7.10 (m, 7H), 7.15–7.17 (m, 1H), 7.22–7.25 (m, 3H); ^{13}C NMR ($CDCl_3$) δ = 29.7, 34.9, 35.7, 124.1 (q, J = 275.9 Hz), 125.8, 127.0, 127.15, 127.20, 127.23, 127.6, 127.7, 128.26, 128.29, 128.4, 128.7, 129.2 (q, J = 29.2 Hz), 130.7, 151.8 (q, J = 3.1 Hz); ^{19}F NMR ($CDCl_3$) δ = −56.0 (s, 3F); IR (KBr) 3060, 3026, 2939, 2864, 1633 cm^{-1}; HRMS calcd. for $C_{24}H_{21}F_3$ (M^+) 366.1595; found, 366.1604.

*4.3.10. (Z)-1-(4-Chlorophenyl)-1,2-diphenyl-3,3-difluoropropene (**1j**)*

Yield: 80%; M.P. 126–128 °C; ^{1}H NMR ($CDCl_3$) δ = 6.40 (t, J = 55.1Hz, 1H), 6.90–6.91 (m, 2H), 7.06–7.09 (m, 3H), 7.21–7.25 (m, 7H), 7.38–7.40 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 113.9 (t, J = 234.7 Hz), 127.6, 127.8, 127.9, 128.8, 130.2, 131.1, 131.2, 133.2 (t, J = 22.5 Hz), 133.4, 134.4, 134.5, 137.8, 140.0, 147.4 (t, J = 9.4 Hz); ^{19}F NMR ($CDCl_3$) δ = −111.3 (d, J = 55.0 Hz, 2F); IR (KBr) 3022, 1591, 1573, 1490, 1442, 1398, 1369 cm^{-1}.; HRMS calcd. for $C_{21}H_{15}ClF_2$ (M^+) 340.0830; found, 340.0835.

*4.3.11. (Z)-1-(4-Chlorophenyl)-1,2-diphenyl-3,3,4,4,5,5-hexafluoropentene (**1k**)*

Yield: 73%; ^{1}H NMR ($CDCl_3$) δ = 5.79 (tt, J = 52.3, 5.7 Hz, 1H), 6.90–6.92 (m, 2H), 7.01–7.05 (m, 3H), 7.17–7.18 (m, 3H), 7.23–7.26 (m, 4H), 7.31–7.33 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 107.8 (tt, J = 253.2, 31.0 Hz), 110–120 (m, 2*C*), 127.3, 127.8, 127.9, 128.1, 129.15, 129.18, 131.7, 133.4, 134.9, 139.3, 141.3, 151.6 (t, J = 4.1 Hz); ^{19}F NMR ($CDCl_3$) δ = −138.0 ∼ −137.1 (m. 2F), −126.7 ∼ −126.5 (m, 2F), −102.9 ∼ −102.8 (m, 2F); IR (neat) 3058, 1492, 1444, 1398, 1271 cm^{-1}; HRMS calcd. for $C_{23}H_{15}ClF_6$ (M^+) 440.0766; found, 440.0760.

*4.3.11.1. (Z)-1-(4-Chlorophenyl)-1-(4-methoxyphenyl)-2-phenyl-3,3,3-trifluoropropene (**1A′**) (Z)-1-(4-chlorophenyl)-2-(4-methoxyphenyl)-1-phenyl-3,3,3-trifluoropropene (**1A**) (**1A** + **1A′**).* Yield: 76% (determined by ^{19}F NMR); The physical data was described below.

*4.3.12. (Z)-1-(4-Chlorophenyl)-2-(4-methylphenyl)-1-phenyl-3,3,3-trifluoropropene (**1B′**)*

^{1}H NMR ($CDCl_3$) δ = 2.27 (s, 3H), 7.01 (d, J = 7.9 Hz, 2H), 7.10 (d, J = 7.9 Hz, 2H); ^{19}F NMR ($CDCl_3$) δ = –56.3 (s, 3F); ^{13}C NMR ($CDCl_3$) δ = 21.2, 123.5 (q, J = 275.7 Hz), 148.7 (q, J = 3.5 Hz).

*4.3.13. (Z)-1-(4-Chlorophenyl)-1-(4-methylphenyl)-2-phenyl-3,3,3-trifluoropropene (**1B**)*

^{1}H NMR ($CDCl_3$) δ = 2.17 (s, 3H), 6.75 (d, J = 8.2 Hz, 2H), 6.84 (d, J = 8.0 Hz, 2H); ^{19}F NMR ($CDCl_3$) δ = −56.1 (s, 3F); ^{13}C NMR ($CDCl_3$) δ = 21.1, 148.9 (q, J = 3.1 Hz).

(*1B* + *1B′*). Yield: 89% (Determined by ^{19}F NMR); ^{1}H NMR ($CDCl_3$) δ = 6.88–7.34 (m, 18H); ^{13}C NMR ($CDCl_3$) δ = 127.5, 127.8, 127.9, 128.0, 128.23, 128.26, 128.29, 128.5, 128.7, 129.66, 129.70, 130.0, 131.1, 131.29, 131.33, 131.7, 133.9, 134.9, 135.6, 137.5, 137.8, 139.1, 139.2, 140.7; IR (neat) 3028, 2923, 2868, 1903, 1593, 1577, 1512 cm^{-1}; HRMS calcd. for $C_{22}H_{16}ClF_3$ (M^+) 372.0893; found, 372.0888.

*4.3.14. Ethyl 4-((Z)-1-(4-chlorophenyl)-2-phenyl-3,3,3-trifluoropropenyl)benzoate (**1C**)*

^{1}H NMR ($CDCl_3$) δ = 1.36 (t, J = 7.2 Hz, 3H), 4.34 (q, J = 7.1 Hz, 2H), 7.36 (d, J = 8.5 Hz, 3H), 7.89 (d, J = 8.3 Hz, 2H); ^{19}F NMR ($CDCl_3$) δ = –56.0 (s, 3F); ^{13}C NMR ($CDCl_3$) δ = 14.2, 61.1, 123.2 (q, J = 275.5 Hz), 129.1 (q, J = 28.8 Hz), 150.0 (q, J = 3.0 Hz), 166.1.

*4.3.15. Ethyl 4-((Z)-2-(4-chlorophenyl)-2-phenyl-1-trifluoromethyl-ethenyl)benzoate (**1C′**)*

^{1}H NMR ($CDCl_3$) δ = 1.32 (t, J = 7.1 Hz, 3H), 4.28 (q, J = 7.1 Hz, 2H), 7.31 (d, J = 8.1 Hz, 3H), 7.73 (d, J = 8.3 Hz, 2H); ^{19}F NMR ($CDCl_3$) δ = –56.6 (s, 3F); ^{13}C NMR ($CDCl_3$) δ = 14.2, 61.0, 123.2 (q, J = 276.2 Hz), 148.1 (q, J = 3.0 Hz), 165.9.

(*1C* + *1C′*). Yield: 76% (determined by ^{19}F NMR); ^{1}H NMR ($CDCl_3$) δ = 6.87–7.25 (m, 16H); ^{13}C NMR ($CDCl_3$) δ = 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 129.1, 129.2, 129.4, 129.5, 129.6, 129.82, 129.84, 129.88, 129.90, 131.1, 131.3, 134.1, 134.2, 134.3, 138.1, 138.5, 139.4, 140.0, 145.0; IR (neat) 2983, 2906, 1716, 1608, 1593 cm^{-1}; HRMS calcd. for $C_{24}H_{18}O_2ClF_3$ (M^+) 430.0947; found, 430.0948.

*4.3.16. (Z)-1-(4-Chlorophenyl)-1-(3-methoxyphenyl)-2-phenyl-3,3,3-trifluoropropene (**1D**)*

^{1}H NMR ($CDCl_3$) δ = 3.69 (s, 3H), 6.81 (d, J = 7.6 Hz, 1H); ^{19}F NMR ($CDCl_3$) δ = −56.1 (s, 3F); ^{13}C NMR ($CDCl_3$) δ = 55.1, 123.4 (q, J = 275.9 Hz), 149.0 (q, J = 3.0 Hz), 159.1.

*4.3.17. (Z)-1-(4-Chlorophenyl)-2-(3-methoxyphenyl)-1-phenyl-3,3,3-trifluoropropene (**1D′**)*

^{1}H NMR ($CDCl_3$) δ = 3.54 (s, 3H), 6.46 (d, J = 7.7 Hz, 1H), 6.59 (dd, J = 8.2, 2.5 Hz, 1H), 6.96 (t, J = 7.9 Hz, 1H); ^{19}F NMR ($CDCl_3$) δ = –56.2 (s, 3F); ^{13}C NMR ($CDCl_3$) δ = 55.0, 123.4 (q, J = 275.4 Hz), 148. (q, J = 3.4 Hz), 158.8.

(*1D* + *1D′*). Yield: 84% (Determined by ^{19}F NMR); ^{1}H NMR ($CDCl_3$) δ = 6.41–7.35 (m, 22H); ^{13}C NMR ($CDCl_3$) δ = 112.8, 113.4, 113.7, 115.3, 117.0, 122.3, 123.8, 127.6, 127.8, 128.0, 128.3, 128.8, 128.9, 129.4, 129.9, 131.2, 134.0, 134.7, 135.0, 135.8, 138.7, 138.8, 140.5, 141.6; IR (neat) 2914, 2835, 1577, 1488, 1465 cm^{-1}; HRMS calcd. for $C_{22}H_{16}OClF_2$ (M^+) 388.0842; found, 388.0844.

*4.3.18. (Z)-1-(4-Chlorophenyl)-1-(2-methoxyphenyl)-2-phenyl-3,3,3-trifluoropropene (**1E**)*

^{1}H NMR ($CDCl_3$) δ = 3.65 (s, 3H), 6.61 (d, J = 8.3 Hz, 1H), 6.68 (t, J = 7.4 Hz, 1H), 6.88 (d, J = 7.5 Hz, 1H); ^{19}F NMR ($CDCl_3$) δ = −56.4 (s, 3F); ^{13}C NMR ($CDCl_3$) δ = 55.1, 123.3 (q, J = 275.5 Hz), 131.2 (q, J = 28.8 Hz), 146.5 (q, J = 3.5 Hz).

*4.3.19. (Z)-1-(4-Chlorophenyl)-2-(2-methoxyphenyl)-1-phenyl-3,3,3-trifluoropropene (**1E′**)*

^{1}H NMR ($CDCl_3$) δ = 1.76 (s, 3H); ^{19}F NMR ($CDCl_3$) δ = −56.93 (s, 3F); ^{13}C NMR ($CDCl_3$) δ = 55.5, 131.7 (q, J = 28.4 Hz).

(*1E* + *1E′*). Yield: 60% (determined by ^{19}F NMR); ^{1}H NMR ($CDCl_3$) δ = 6.77–7.34 (m, 23H); ^{13}C NMR ($CDCl_3$) δ = 110.6, 110.8, 120.2, 120.2, 124.1, 127.5, 127.6, 127.8, 127.9, 128.2, 128.5, 129.0, 129.5, 129.9, 130.0, 130.1, 132.1, 133.4, 133.8, 134.8, 138.3, 138.7, 140.8, 155.5, 158.2; IR (neat) 3058, 3026, 3004, 2937, 2837, 1596, 1581, 1487, 981 cm^{-1}; HRMS calcd. for $C_{22}H_{16}OClF_3$ (M^+) 388.0842; found, 388.0838.

4.4. Determination of the stereochemistry

4.4.1. General procedure for the reaction of fluoroalkylated acetylene derivatives with organocopper reagents

To a solution of CuCN (94 mg, 1.05 mmol) and 1-(4-chlorophenyl)-3,3,3-trifluoropropyne (175 mg, 0.86 mmol) in THF (8 mL) was added Grignard reagent (2.10 mmol) at −45 °C. After stirring for 10 min, the reaction mixture was allowed to warm to −5 °C and then stirred for 30 min. The reaction mixture was again cooled to −45 °C. After stirring at that temperature for 2 h, iodine (533 mg, 2.50 mmol) in THF (4 mL) was added slowly. After 1h, the reaction was quenched with MeOH/NH_3 aq. and a few drops of Na_2SO_3 were added until the color of the reaction mixture changed. The whole was extracted with EtOAc three times. The combined organic layers were washed with NaCl aq., dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography to give the corresponding vinyl iodide.

*4.4.1.1. (Z)-1-(4-Chlorophenyl)-2-iodo-1-phenyl-3,3,3-trifluoropropene (**5a**).* ^{1}H NMR ($CDCl_3$) δ = 3.81 (3H, s), 6.87 (2H, d, J = 8.2 Hz), 7.13–7.17 (4H, m), 7.30–7.31 (3H, m); ^{19}F NMR ($CDCl_3$) δ = –54.21 (3F, s); ^{13}C NMR ($CDCl_3$) δ = 55.2, 85.2 (q, J = 34.2 Hz), 113.7, 121.4 (q, J = 270.5 Hz), 128.1, 128.1, 129.8, 137.7, 139.7, 158.6 (q, J = 3.2 Hz), 160.8; IR (neat) 1604, 1508, 1461 cm^{-1}; HRMS (FAB) calcd. for $C_{16}H_{12}F_3IO$ (M^+) 403.9885; found, 403.9889; Anal. calcd. C, 47.55; H, 2.99; found, C, 47.54; H, 2.71.

*4.4.1.2. (Z)-1-(4-Chlorophenyl)-2-iodo-1-(4-methoxyphenyl)-3,3,3-trifluoropropene (**6a**).* Yield: 46%; ^{1}H NMR ($CDCl_3$) δ = 3.82 (s, 3H), 6.89 (d, J = 8.6 Hz, 2H), 7.13 (t, J = 8.9 Hz, 4H), 7.30 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 55.2, 85.7 (q, J = 34.3 Hz), 113.8, 121.3 (q, J = 273.9 Hz), 128.4, 129.5, 129.9, 134.6, 137.2, 138.0, 157.3 (q, J = 3.4 Hz), 159.9; ^{19}F NMR ($CDCl_3$) δ = −54.1 (s, 3F); IR (neat) 2960, 2839, 1604, 1589, 1508, 1487 cm^{-1}; HRMS calcd. for $C_{16}H_{11}ClF_3IO$ (M^+) 437.9495; found, 437.9495.

4.4.2. General procedure for the Suzuki-Miyaura cross-coupling reaction

To a solution of the vinyl iodide (0.37 mmol) and $Pd(PPh_3)_4$ (45 mg, 0.036 mmol) in benzene (7 mL) was added Na_2CO_3 (97 mg, 0.91 mmol), aryl boronic acid (1.46 mmol), H_2O (0.45 mL), and EtOH (0.45 mL). The reaction mixture was refluxed for 12 h, and then quenched with sat. NH_4Cl aq. The whole was extracted with EtOAc three times. The combined organic layers were washed with NaCl aq., dried over anhydrous Na_2SO_4, and then concentrated in vacuo. The residue was purified by silica gel column chromatography to give the corresponding fluorine-containing tetrasubstituted alkene.

*4.4.2.1. (Z)-1-(4-Chlorophenyl)-2-(4-methoxyphenyl)-1-phenyl-3,3,3-trifluoropropene (**1A**).* Yield: 77% (determined by ^{19}F NMR); M.P. 131–133 °C; ^{1}H NMR ($CDCl_3$) δ = 3.75 (s,

3H), 6.74 (d, J = 8.7 Hz, 2H), 6.88–6.91 (m, 2H), 7.05–7.08 (m. 3H), 7.14 (d, J = 8.3 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 55.1, 113.5, 123.6 (q, J = 275.5 Hz), 126.9, 127.4, 127.8, 128. 25, 128.31, 129.5 (q, J = 28.9 Hz), 129.7, 130.0, 132.6, 133.9, 139.1, 140.7, 148.7 (q, J = 3.5 Hz), 159.2; ^{19}F NMR ($CDCl_3$) δ = –56.4 (s, 3F); IR (KBr) 3003, 1610, 1577, 1512, 1487, 1465 cm^{-1}; HRMS calcd. for $C_{22}H_{16}ClF_3O$ (M^+) 388.0842; found, 388.0845.

*4.4.2.2. (Z)-1-(4-Chlorophenyl)-1-(4-methoxyphenyl)-2-phenyl-3,3,3-trifluoropropene (**1A′**).* Yield: 82%; ^{1}H NMR ($CDCl_3$) δ = 3.68 (s, 3H), 6.55 (d, J = 8.8 Hz, 2H), 6.78 (d, J = 8.8 Hz, 2H), 7.21–7.23 (m, 7H), 7.33 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 55.0, 113.1, 123. (q, J = 275.2 Hz), 127.9, 128.1, 128.2, 128.3, 128.8 (q, J = 28.5 Hz), 130.1, 131.4, 132.7, 133.9, 135.1, 139.3, 148.5 (q, J = 3.0 Hz), 158.9; ^{19}F NMR ($CDCl_3$) δ = −55.8 (s, 3F); IR (neat) 2935, 2910, 2839, 1604, 1573 cm^{-1}; HRMS calcd. for $C_{22}H_{16}ClF_3O$ (M^+) 388.0842; found, 388.0846.

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