Available online at www.sciencedirect.com
SCIENCE DIRECT
Journal of Fluorine Chemistry 127 (2006) 36–43
JOURNAL OF FLUORINE CHEMISTRY
www.elsevier.com/locate/fluor

Highly regio- and stereoselective hydrometallation reactions of fluorine-containing internal alkynes: Novel approaches to fluoroalkylated alkenes

Tsutomu Konno *, Jungha Chae, Tomoo Tanaka, Takashi Ishihara, Hiroki Yamanaka

Department of Chemistry and Materials Technology, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606-8585, Japan

Received 7 September 2005; received in revised form 26 September 2005; accepted 28 September 2005
Available online 11 November 2005

Abstract

Hydroalumination, hydrocupration, and hydroboration reactions of various fluorine-containing alkynes were investigated. The alkyne reacted smoothly with 2.0 equiv. of Red-Al at −78 °C to give the hydroaluminated adduct in a highly regio- and stereoselective manner, which was treated with iodine, the corresponding vinyliodide being produced in moderate yield. Hydrocupration of the alkynes also took place, but the resulting vinylmetal reacted with various electrophiles sluggishly. In sharp contrast, the reaction with dicyclohexylborane proceeded smoothly to afford the *cis*-addition products preferentially, which were subjected to Suzuki-Miyaura cross-coupling reaction, leading to trisubstituted alkenes in high yields.

Keywords: Fluorine-containing alkynes; Hydroalumination; Hydrocupration; Hydroboration; Suzuki-Miyaura cross-coupling

1. Introduction

Recently, much interest has been focused on organofluorine compounds as pharmaceutical and agrochemical agents because the fluorine atom often alters the physiochemical properties of organic compounds, thereby modifying biological activities [1]. Accordingly, the development of novel and convenient methods for the synthesis of fluorine-containing molecules has been becoming more and more important in fluorine chemistry [2]. Among various types of fluorinated molecules, alkenes possessing a fluoroalkyl group are well known as one of the most important synthetic targets because they are often found in the framework of biologically active compounds, such as panomifene [3]. Although several synthetic methods for such molecules have been reported thus far [4], the hydrometallation of fluoroalkylated alkynes is potentially very attractive because the hydrometallation reaction very often proceeds in a highly regio- and stereoselective fashion and the resulting vinylmetal intermediates can be converted further to variously substituted ethenes under the influence of transition metal catalyst with retention of configuration [5]. Despite of such great utility, little attention has been paid to such reaction of fluorine-containing alkynes so far [6]. Herein, we wish to describe highly regio- and stereoselective hydrometallation reactions of various fluoroalkylated alkynes in detail.

2. Results and discussion

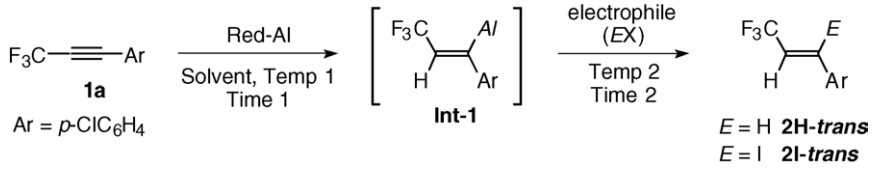
2.1. Hydroalumination [7]

Initially, the hydroalumination reaction of trifluoromethylated internal alkyne **1a** [8] with Red-Al was examined (Table 1). Thus, treatment of **1a** with 1.2 equiv. of Red-Al in toluene at −78 °C for 4 h, followed by quenching the reaction with H_2O, gave the corresponding trifluoromethylated alkene **2H-*trans*** in 56% yield as a sole product, together with 44% of the starting material (Entry 1). In this case, no stereoisomer **2H-*cis*** (Fig. 1) was detected at all. Changing the solvent from toluene to ether led to a significant increase of the yield as shown in Entry 3, though no influence was observed in the reaction in THF (Entry 2). The reaction at −45 °C was also found to be satisfactory (Entry 4), but higher reaction temperature resulted in a decrease of the yield (Entry 5). The use of 2.0 equiv. of Red-Al brought about the optimum yield,

* Corresponding author.

0022-1139/$ – see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.jfluchem.2005.09.015

Table 1
Hydroalumination of trifluoromethylated internal alkyne with Red-Al



Entry	Equiv. of Red-Al	Solvent	Temperature 1 (°C)	Time 1 (h)	Electrophile (equiv.)	Temperature 2 (°C)	Time 2 (h)	Yield[a] (%) of **2H-*trans***	Recovery[a] (%) of **1a**	Yield[a] (%) of **2I-*trans***
1	1.2	Ph–Me	−78	4	H_2O (excess)	−78	1	56	44	–
2	1.2	THF	−78	4	H_2O (excess)	−78	1	47	0	–
3	1.2	Et_2O	−78	4	H_2O (excess)	−78	1	86	14	–
4	1.2	Et_2O	RT	4	H_2O (excess)	RT	1	64	0	–
5	1.2	Et_2O	−45	4	H_2O (excess)	−45	1	83	3	–
6	2.0	Et_2O	−78	4	H_2O (excess)	−78	1	95	4	–
7	2.0	Et_2O	−78	8	H_2O (excess)	−78	1	94	1	–
8	2.0	Et_2O	−78	4	I_2 (6.0)	−50 → RT	2	82	Trace	15
9	2.0	Et_2O	−78	4	I_2 (6.0)	RT	2	56	Trace	32
10	2.0	Et_2O	−78	4	I_2 (6.0)	RT → refl.	2	33	Trace	48
11	2.0	Et_2O	−78	4	I_2 (6.0)	Refl.	2	33	Trace	55
12	2.0	Et_2O	−78	4	I_2 (6.0)	Refl.	6	32	Trace	66
13	2.0	Et_2O	−78	4	I_2 (12.0)	Refl.	6	36	Trace	50

[a] Determined by ^{19}F NMR.

2H-*trans* being afforded in 95% yield, though 4% of **1a** still remained unreacted. The prolonged reaction time did not lead to the complete consumption of the starting alkyne (Entry 7).

With this optimized reaction conditions, we next examined the iodination of the hydroaluminated intermediate **Int-1** as described in Entries 8–13. Treatment of **Int-1** with 6.0 equiv. of iodine at −50 °C, followed by warming the reaction from −50 °C to RT over 2 h, gave the desired vinyliodide **2I-*trans***, exclusively, in only 15% yield, together with 82% recovery of the protonated **2H-*trans*** (Entry 8). The iodination at room temperature resulted in the increase of the yield from 15% to 32% yield (Entry 9). Additionally, the refluxing conditions (Entries 10 and 11) as well as the prolonged reaction time (Entry 12) led to the increase of the yield. It should be noted that the use of 12.0 equiv. of iodine caused a slight decrease of the yield from 66% to 50% (Entry 13). Further investigation to improve the yield of **2I-*trans*** did not lead to the satisfactory results. In all cases, **2H-*trans*** and **2I-*trans*** were inseparable by silica gel column chromatography. Additionally, the regioisomers, **3I-*cis*** and **3I-*trans***, were not detected at all (Fig. 1).

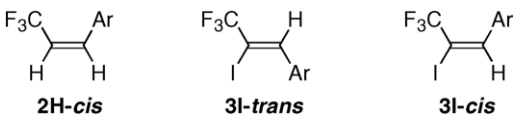


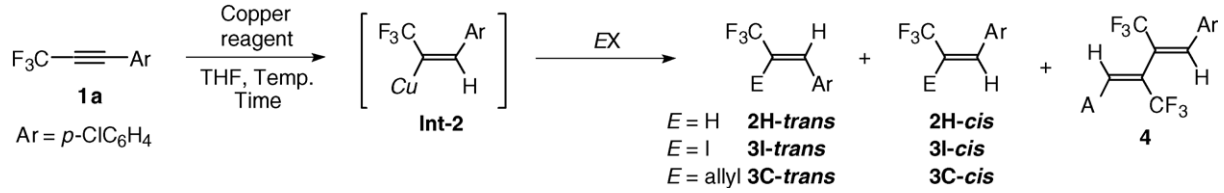
Fig. 1. The regio- and stereoisomers.

2.2. Hydrocupration [9]

We next examined the hydrocupration reaction with copper hydride, which was prepared from copper bromide and Red-Al (Table 2). As described in Entry 1, copper hydride was found to be inactive, the starting material being recovered quantitatively. On the other hand, the reaction with $[CuH_2]^-$ at −45 °C for 4 h took place in a preferential *cis*-addition manner to give **2H-*trans*** and **2H-*cis*** in 59% yield in a ratio of 22:78, after quenching the reaction with H_2O (Entry 2). Changing the reaction temperature from −45 °C to −78 °C caused an increase of the stereoselectivity, **2H-*cis*** being obtained as a single isomer, though the chemical yield was decreased significantly (Entry 3). The use of 2.4 equiv. of $[CuH_2]^-$ at −78 °C brought about a dramatical improvement of the yield from 19% to 69% (Entry 4). Though the prolonged reaction time did not lead to a satisfactory result, the reaction with 3.6 equiv. of $[CuH_2]^-$ at −78 °C for 4 h gave a good yield as well as an excellent stereoselectivity (Entry 6).

With this reaction conditions, we attempted the reaction of **Int-2** with various electrophiles as shown in Entries 7–9. Treatment of **Int-2** with 9.6 equiv. of iodine at −78 °C for 4 h gave the corresponding vinyl iodide **3I-*cis*** in 41% yield. In sharp contrast to the hydroalumination reaction, only the compounds possessing the iodine atom at the carbon attached with a CF_3 group were obtained exclusively. No other regioisomers were detected at all. Similarly, the allylation reaction of **Int-2** using allyl bromide proceeded sluggishly to afford the corresponding allylated product **3C-*cis*** in only 31% yield, whereas benzyl bromide was found to be completely inactive.

Table 2
Hydrocupration reaction of trifluoromethylated alkynes



Entry	Copper reagent	Equiv.	Temperature (°C)	Time (h)	EX (equiv.)	Yield[a] (%) of **2** or **3**	Ratio (*trans*:*cis*)	Yield[a] (%) of **4**	Recovery[a] (%) of **1a**
1	CuH	1.2	−45	4	H_2O (excess)	0	–	0	100
2	CuH_2	1.2	−45	4	H_2O (excess)	59	22:78	10	5
3	CuH_2	1.2	−78	4	H_2O (excess)	19	0:100	1	66
4	CuH_2	2.4	−78	4	H_2O (excess)	69	4:96	1	12
5	CuH_2	2.4	−78	8	H_2O (excess)	58	8:92	7	3
6	CuH_2	3.6	−78	4	H_2O (excess)	69	1:99	8	0
7	CuH_2	3.6	−78	4	I_2 (9.6)	41	1:99	N.D.	0
8	CuH_2	3.6	−78	4	BnBr (9.6)	0	1:99	N.D.	0
9	CuH_2	3.6	−78	4	Allylbromide (9.6)	31	1:99	N.D.	0

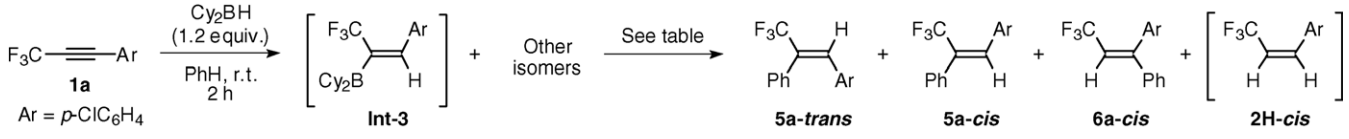
[a] Determined by ^{19}F NMR.

2.3. Hydroboration [10]

Additionally, we investigated the hydroboration reaction of **1a** with dicyclohexylborane was examined. On treating **1a** with 1.2 equiv. of dicyclohexylborane (prepared by the reaction of cyclohexene (2.4 equiv.) with borane THF complex (1.2 equiv.) in benzene at room temperature for 2 h), the vinylborane **Int-3** was formed selectively, together with a small amount of other isomers (<10%). This encouraged us to examine the subsequent cross-coupling reaction without isolation of vinylborane **Int-3** (Table 3). Thus, a benzene solution of the vinylborane **Int-3** was treated with 1.2 equiv. of iodobenzene, 5 mol% of $Pd(PPh_3)_4$, and 3.0 equiv. of NaOEt, and the whole was refluxed for 4 h. After quenching the reaction with acetic acid, ^{19}F NMR analysis indicated that the desired coupling products **5a** and **6a** was formed in 23% yield, together with 76% of **2H-*cis*** (Entry 1). Prolonged reaction time led to the significant decrease of the yield (Entry 2). Switching the palladium catalyst from $Pd(PPh_3)_4$ to $Pd(PPh_3)_2Cl_2$ brought about a slight increase of the yield (Entry 3). It is interesting to note that the base used in this reaction was crucial for the high yield. Thus, changing the base from NaOEt to NaOH resulted in the dramatical increase of the yield as described in Entry 4. In this case, 10% of **2H-*cis*** was recovered unchanged. The use of 10.0 mol% of the palladium catalyst led to the complete consumption of the vinylborane **Int-3**, giving the desired product in 89% yield (Entry 5). In Entries 4 and 5, the high regioselectivity (**5a-*trans*** + **5a-*cis***:**6a-*cis*** = 94:6) and the high stereoselectivity (**5a-*trans***:**5a-*cis*** = 2:98) were observed.

With the optimized reaction conditions in hand, the scope of the one-pot reaction was investigated with various alkynes in detail (Table 4). As shown in Entries 1–4 and 6, various types of alkynes carrying an electron-donating group (Me, MeO) or an

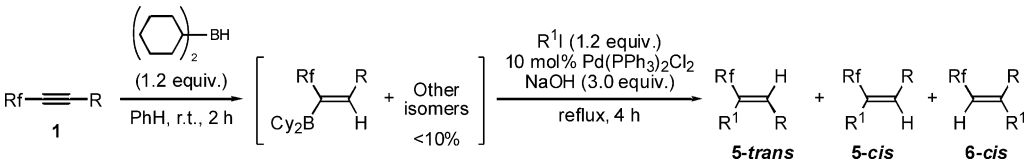
Table 3
Hydroboration reaction of trifluoromethylated alkyne



Entry	Catalyst[a]	Base	Time (h)	Yield[b,c] (%) of **5a** + **6a**	Ratio[b] **5a** (*trans*:*cis*):**6a-*cis***	Yield[b] (%) of **2H-*cis***
1	$Pd(PPh_3)_4$	NaOEt	4	23	N.D.[a]	76
2	$Pd(PPh_3)_4$	NaOEt	20	7	N.D.[a]	35
3	$Pd(PPh_3)_2Cl_2$	NaOEt	4	37	N.D.[a]	63
4	$Pd(PPh_3)_2Cl_2$	NaOH	4	80	94 (2:98):6	10
5	$Pd(PPh_3)_2Cl_2$[d]	NaOH	4	89 (64)	94 (2:98):6	0

[a] Unless otherwise noted, all reaction were employed in the presence of 5 mol% of catalyst.
[b] Determined by ^{19}F NMR.
[c] Value in parentheses is of isolated yield.
[d] Ten mol% of $Pd(PPh_3)_2Cl_2$ was employed.

Table 4
The synthesis of a variety of trisubstituted alkenes



Entry	Rf	R	R^1	Yield[a] (%) of **5** + **6**	Product	**5** (*cis*:*trans*):**6**
1	CF_3	Ph	Ph	85 (73)	**b**	95 (0:100):5
2	CF_3	*p*-ClC_6H_4	Ph	89 (64)	**a**	94 (2:98):6
3	CF_3	*p*-MeC_6H_4	Ph	83 (66)	**c**	94 (0:100):6
4	CF_3	*p*-$MeOC_6H_4$	Ph	99 (88)	**d**	96 (0:100):4
5	CF_3	*p*-$O_2NC_6H_4$	Ph	25	**e**	88 (0:100):12
6	CF_3	*p*-$EtO_2CC_6H_4$	Ph	99	**f**	95 (0:100):5
7	CF_3	*p*-$MeOC_6H_4CH_2$	Ph	62[b]	**g**	58 (0:100):42
8	CF_3	*p*-ClC_6H_4	*o*-ClC_6H_4	53[c]	**h**	92 (0:100):8
9	CF_3	*p*-ClC_6H_4	*m*-ClC_6H_4	74	**i**	93 (0:100):7
10	CF_3	*p*-ClC_6H_4	*p*-ClC_6H_4	83 (74)	**j**	96 (0:100):4
11	CF_3	*p*-ClC_6H_4	*p*-MeC_6H_4	86 (55)	**k**	94 (1:99):6
12	CF_3	*p*-ClC_6H_4	*p*-$MeOC_6H_4$	68 (56)	**l**	98 (7:93):2
13	CF_3	*p*-ClC_6H_4	*p*-$O_2NC_6H_4$	54	**m**	100 (9:91):0
14	CF_3	*p*-ClC_6H_4	*p*-$EtO_2CC_6H_4$	99	**n**	91 (0:100):9
15	CHF_2	*p*-ClC_6H_4	Ph	67	**o**	84 (0:100):16
16	$HCF_2CF_2CF_2$	*p*-ClC_6H_4	Ph	78	**P**	83 (0:100):17

[a] Determined by ^{19}F NMR. Values in parentheses are of isolated yields.
[b] The product 6 was obtained in 26% yield, together with 8% of 1.
[c] The dimmer 7 was obtained in 20% yield.

electron-withdrawing group (EtO_2C) on the benzene ring could participate well in the reaction to give the corresponding trisubstituted alkenes in high yields. However, a significant decrease of the yield was observed when the alkyne having a nitro group on the benzene ring was used (Entry 5). The regioselectivity was also decreased slightly. Additionally, the fluoroalkylated alkyne having an aliphatic side chain (*p*-$MeOC_6H_4CH_2$–) was not a good substrate, the low regioselectivity (**5**:**6** = 58:42) being obtained and **7** being produced in 26% yield (Entry 7, Fig. 2). We also examined the effect of the coupling reagents (R^1I) on the reaction as shown in Entries 8–14. The position of the substituent on the benzene ring significantly influenced on the coupling reaction. Thus, the dimer **8** was formed in 20% yield when *o*-chloroiodobenzene was used as R^1I (Entry 8, Fig. 2), while the satisfactory result was obtained in the case of *m*-chloroiodobenzene. The reaction using the coupling reagents having various types of substituents, such as chloro, methyl, methoxy, and ethoxycarbonyl groups, proceeded smoothly to afford the trisubstituted alkenes in a highly regio- and stereoselective manner (Entries 10–12 and 14). However, the use of *p*-nitroiodobenzene resulted in the decrease of the yield (Entry 13). It should also be noted that changing the fluoroalkyl group from a trifluoromethyl group to a difluoromethyl or hexafluoropropyl group did not cause the significant influence on the reaction (Entries 15 and 16).

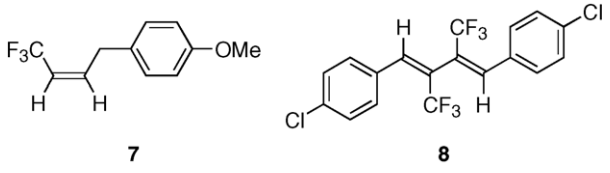
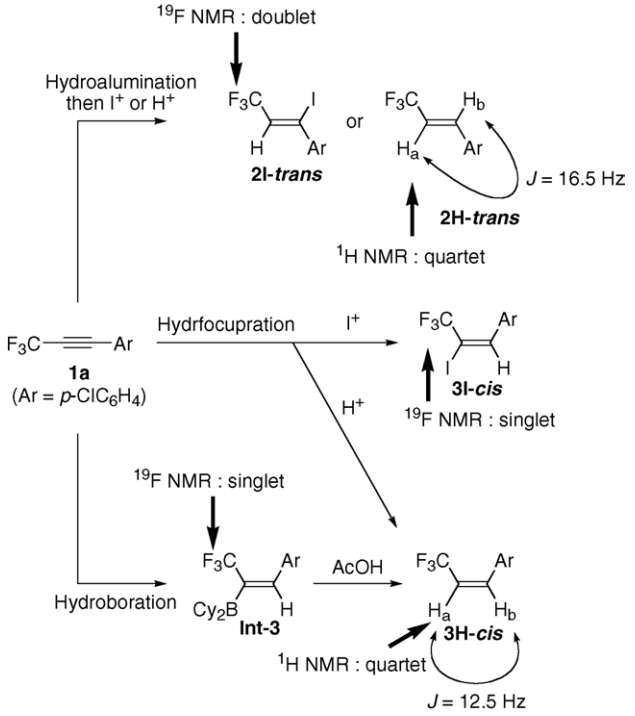


Fig. 2. The byproducts **7** and **8**.

2.4. Stereochemistry

The stereochemical outcome of the reactions was made as follows (Scheme 1). Thus, ^{19}F NMR analysis of **2I-*trans*** (prepared readily from the hydroalumination of **1a** and the subsequent iodination) showed a doublet peak, indicating that the iodine atom is attached to a carbon distal to a CF_3 group. Additionally, the analysis of the ^1H NMR of **2H-*trans*** (obtained by the hydroalumination followed by quenching the reaction with H_2O) showed the coupling constant of H_a and H_b to be 16.5 Hz. This strongly indicates that **2H-*trans*** has the *E* configuration. Similarly, ^{19}F NMR analysis of **3I-*cis*** (prepared by the hydrocupration of **1a**) and **Int-3** showed a singlet peak, strongly suggesting that the iodine atom or a dicyclohexylboryl group is attached to a carbon possessing a CF_3 group. Furthermore, the acid hydrolysis of **Int-2** or **Int-3** led to the corresponding alkene, which showed the H_a–H_b coupling constant to be 12.5 Hz, indicating that the hydrolysis products have the *Z* configuration.

Accordingly, it was revealed that the hydroalumination proceeded in a high *trans* addition manner, whereas the hydrocupration and hydroboration took place in a high *cis* addition manner. Furthermore, the hydroalumination was found



Scheme 1. Determination of the stereochemistry.

to be opposite to the hydrocupration and the hydroboration in the regioselectivity.

3. Conclusion

In summary, we have investigated three types of hydrometallation reactions of various fluorine-containing alkynes in detail. Hydroalumination or hydrocuprataion proceeded smoothly in a *trans* or *cis* addition manner, respectively, to give the corresponding vinyl metal intermediates. The intermediates reacted smoothly with H^+, *trans*-, or *cis*-disubstituted alkenes being obtained in good to high yields. However, the reaction of the intermediates with the other electrophiles, such as allylbromide, benzylbromide, and so on, took place sluggishly. On the other hand, hydroboration occurred in a highly regio- and stereoselective fashion, followed by the subsequent Suzuki-Miyaura cross-coupling reaction, affording the trisubstituted alkenes in excellent yields.

4. Experimental

4.1. General experimental procedures

^{1}H 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 used for determining regioselectivity and stereoselectivity and was used for taking ^{19}F NMR spectra in a $CDCl_3$ solution with internal $CFCl_3$ too. $CFCl_3$ 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. Gas chromatography (GC) was taken on a Shimadzu GC-7AG. Gas chromatography mass spectra (GS–MS) were taken on a Shimadzu GCMS-QP1000.

4.1.1. Materials

Tetrahydrofuran (THF), copper bromide and iodine were commercially available from Wako Chemicals Co. Red-Al (1.6 M hexane solution) was purchased from Aldrich Chemicals Co. Toluene, benzene, Et_2O, and cyclohexene were freshly distilled from calcium hydride (CaH_2). 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 a previous literature procedure.

4.2. The reaction of hydroaluminated adduct with iodine

To a solution of Red-Al (0.12 mL, 0.40 mmol, 3.3 M toluene solution) in ether (2 mL) was added 1-(4-chlorophenyl)-3,3,3-trifluoropropyne (41 mg, 0.20 mmol) at −78 °C and the whole was stirred for 4 h at −78 °C. Then, a THF solution of I_2 (305 mg, 1.20 mmol) (2.4 mL) was added to the reaction mixture at −78 °C and gradually warmed up to the reflux temperature. The whole was refluxed for 6 h and then cooled to room temperature. Then the mixture was quenched with aqueous $NaHCO_3$ and Na_2SO_3, extracted with ethyl acetate three times. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica gel to give the corresponding vinyl iodide with some impurities.

4.2.1. (Z)-1-(4-Chlorophenyl)-3,3,3-trifluoro-1-iodo-1-propene (*2I-trans*)

Only identified peaks were noted as follows. ^{1}H NMR ($CDCl_3$) δ 6.56 (1H, q, J = 7.22 Hz), 7.35 (2H, d, J = 8.60 Hz), 7.43 (2H, d, J = 8.64 Hz); ^{19}F NMR; δ −60.8 (3F, d, J = 6.50 Hz).

4.2.2. The reaction of hydrocuprated adduct with iodine

To a solution of copper bromide (144 mg, 1.00 mmol) in THF (4 mL) was added 0.30 mL of Red-Al (1.00 mmol, 3.3 M toluene solution) at −45 °C. The whole was stirred for 30 min, then cooled to −78 °C. To this mixture was added 1-(4-chlorophenyl)-3,3,3-trifluoropropyne (57 mg, 0.28 mmol) and the solution was stirred at −78 °C. After stirring for 4 h, a THF solution of I_2 (683 mg, 2.69 mmol) (2 mL) was added to the reaction mixture and the whole was stirred for 4 h at −78 °C, followed by addition of a mixture of MeOH (2 mL) and 25 wt.% aqueous NH_3 solution (2 mL). The whole was stirred for 30 min, then gradually warmed up to room temperature. The reaction was quenched with aqueous $NaHCO_3$ and Na_2SO_3, and

the whole was extracted with ethyl acetate three times. The combined organic layers were dried over anhydrous Na_2SO_4, concentrated in vacuo. The residue was chlomatographed on silica gel to give the corresponding vinyl iodide.

*4.2.2.1. (E)-1-(4-Chlorophenyl)-3,3,3-trifluoro-2-iodo-1-propene (**3I-cis**).* Yield 69% (determined by ^{19}F NMR); ^1H NMR ($CDCl_3$) δ 7.20 (d, J = 8.50 Hz, 2H), 7.34 (d, J = 8.50 Hz, 2H), 7.73 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 84.5 (q, J = 37.4 Hz), 120.6 (q, J = 273.9 Hz), 128.6, 129.4 (q, J = 2.5 Hz), 134.1, 135.2, 148.7 (q, J = 3.1 Hz); ^{19}F NMR ($CDCl_3$) δ −56.9 (s, 3F); IR (neat) 2928, 2854, 1591, 1491, 1354, 1304 cm^{-1}; MS (FAB) *m/z* 221, 205.

4.2.3. The coupling reaction of hydrocuprated adduct with allylbromide

To a solution of copper bromide (144 mg, 1.00 mmol) in THF (4 mL) was added 0.30 mL of Red-Al (1.00 mmol, 3.3 M toluene solution) at −45 °C. The whole was stirred for 30 min, then cooled to −78 °C. To the solution was added 1-(4-chlorophenyl)-3,3,3-trifluoropropyne (57 mg, 0.28 mmol) and the whole was stirred for 4 h at −78 °C. Then allyl bromide (0.23 mL, 2.69 mmol) in THF (2 mL) was added to the reaction mixture and the whole was stirred for 4 h at −78 °C, followed by addition of a mixture of MeOH (2 mL) and 25 wt.% of aqueous NH_3 solution (2 mL). The whole was stirred for 30 min, then gradually warmed up to room temperature, quenched with aqueous $NaHCO_3$, and extracted with ethyl acetate three times. The combined organic layers were dried over anhydrous Na_2SO_4, concentrated in vacuo. The residue was chlomatographed on silica gel to give the corresponding trisubstituted alkene.

*4.2.3.1. (1E)-1-(4-Chlorophenyl)-2-trifluoromethylpenta-1,4-diene (**3C-cis**).* Yield 31% (determined by ^{19}F NMR); ^1H NMR ($CDCl_3$) δ 3.08 (2H, dd, J = 6.76 Hz, 5.48 Hz), 5.20 (1H, t), 5.23 (1H, m), 5.87 (1H, m), 6.71 (1H, s), 7.20 (2H, d, J = 8.42 Hz), 7.30 (2H, d, J = 8.51 Hz); ^{13}C NMR ($CDCl_3$) δ 36.44 (q, J = 2.44 Hz), 118.29, 123.59 (q, J = 275.81 Hz), 128.28, 129.76 (q, J = 2.52 Hz), 129.95 (q, J = 28.55 Hz), 133.46, 133.81, 13.99, 134.52 (q, J = 3.77 Hz); ^{19}F NMR; δ −60.1 (3F, s); IR (neat) 3084, 2984, 2918, 1655, 1643, 1595, 1493, 1435 cm^{-1}.

4.2.4. General procedure for the hydroboration-coupling reaction

To a solution of cyclohexene (0.12 mL, 1.2 mmol) in benzene (2.0 mL) was added 0.58 mL (0.6 mmol) of borane at 0 °C and the whole solution was stirred for 20 min. The color of reaction mixture became white. To this solution was added dropwise 1 (0.5 mmol), and allowed to warm to RT, then stirred for 2 h. After the reaction mixture became clear, iodobenzene (0.12 g, 0.6 mmol), dichlorobis(triphenylphosphine)palladium (0.034 g, 0.05 mmol) and 2.5 M sodium hydroxide (0.57 mL, 1.5 mmol) were added to the reaction mixture and the whole solution was stirred for 4 h at reflux. Then the mixture was quenched with water, and extracted with Et_2O three times. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica gel or TLC plate to afford **5** and **6**.

*4.2.4.1. (Z)-1,2-Diphenyl-3,3,3-trifluoropropene (**5b-cis**).* Yield 84%; mp 55–57 °C; ^1H NMR ($CDCl_3$) δ 7.01 (s, 1H), 7.27–7.40 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 123.4 (q, J = 275.8 Hz), 128.1, 128.2, 128.38, 128.40, 128.60, 128.62, 131.8 (q, J = 30.3 Hz), 134.8, 136.5, 138.9 (q, J = 3.3 Hz); ^{19}F NMR ($CDCl_3$) δ −56.8 (s, 3F); IR (KBr) 2360, 1373, 1218, 1164 cm^{-1}; HRMS calcd. for $C_{15}H_{11}F_3$: 248.0813, found: 248.0818.

*4.2.4.2. (Z)-1-(4-Chlorophenyl)-2-phenyl-3,3,3-trifluoropropene (**5a-cis**).* Yield 68%; ^1H NMR ($CDCl_3$) δ 6.89 (s, 1H), 7.22–7.36 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 123.2 (q, J = 275.6 Hz), 128.1, 128.41, 128.44, 128.6, 130.0, 132.4 (q, J = 30.2 Hz), 133.1, 134.4, 136.2, 137.4 (q, J = 3.2 Hz); ^{19}F NMR ($CDCl_3$) δ −56.84 (s, 3F); IR (neat) 1429, 1377, 1272, 1218, 1168 cm^{-1}; HRMS calcd. for $C_{15}H_{10}{}^{35}ClF_3$: 282.0423, found: 282.0431.

*4.2.4.3. (Z)-1-(4-Methylphenyl)-2-phenyl-3,3,3-trifluoropropene (**5c-cis**).* Yield 79%; ^1H NMR ($CDCl_3$) δ 2.39 (s, 3H), 7.05 (s, 1H), 7.19–7.23 (m, 2H), 7.31–7.35 (m, 2H), 7.37–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 21.3, 123.5 (q, J = 278.3 Hz), 128.2, 128.4, 128.7, 128.9, 130.9 (q, J = 30.2 Hz), 131.8, 136.8, 138.5, 139.0 (q, J = 3.2 Hz); ^{19}F NMR ($CDCl_3$) δ −56.8 (s, 3F); IR (neat) 3028, 1639, 1512, 1447, 1381 cm^{-1}; HRMS calcd. for $C_{16}H_{13}F_3$: 262.0969, found: 262.0974.

*4.2.4.4. (Z)-1-(4-Methoxyphenyl)-2-phenyl-3,3,3-trifluoropropene (**5d-cis**).* Yield 88%; ^1H NMR ($CDCl_3$) δ 3.85 (s, 3H), 6.91–6.96 (m, 2H), 7.00 (s, 1H), 7.36–7.40 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 55.2, 113.6, 122.5 (q, J = 275.0 Hz), 126.9, 128.1, 128.26, 128.33, 129.8 (q, J = 30.3 Hz), 130.6, 137.0, 138.8 (q, J = 3.4 Hz), 159.8; ^{19}F NMR ($CDCl_3$) δ −56.9 (s, 3F); IR (neat) 3063, 2936, 1639, 1512 cm^{-1}; HRMS calcd. for $C_{16}H_{13}F_3O$: 278.0918, found: 278.0912.

*4.2.4.5. (Z)-1-(4-Nitrophenyl)-2-phenyl-3,3,3-trifluoropropene (**5e-cis**).* Yield 25% (determined by ^{19}F NMR); ^1H NMR ($CDCl_3$) δ 7.09 (s, 1H), 7.43–7.48 (m, 5H), 7.55 (d, J = 8.50 Hz, 2H), 8.26 (d, J = 8.50 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 122.92 (q, J = 276.1 Hz), 123.4, 128.0, 128.6, 129.1, 129.36, 129.38, 134.8 (q, J = 30.2 Hz), 135.9 (q, J = 3.4 Hz), 141.5, 147.5; ^{19}F NMR ($CDCl_3$) δ −56.9 (s, 3F); IR (neat) 3109, 2932, 1724, 1601, 1524 cm^{-1}; HRMS calcd. for $C_{15}H_{10}F_3NO_2$: 293.0664, found: 293.0666.

*4.2.4.6. (Z)-Ethyl 4-(3,3,3-trifluoro-2-phenylpropen-1-yl)-benzoate (**5f-cis**).* Yield 88% (chromatographed on TLC plate); ^1H NMR ($CDCl_3$) δ 1.41 (t, 3H, J = 7.50 Hz), 4.4 (q, 2H, J = 7.50 Hz), 7.10 (s, 1H), 7.36–7.50 (m, 6H), 8.03–8.10 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.3, 61.0, 123.1 (q, J = 275.4 Hz), 128.1, 128.5, 128.7, 129.4, 129.5, 130.2, 133.3 (q, J = 31.4 Hz), 136.0, 137.5 (q, J = 3.3 Hz), 139.3,

166.2; ^{19}F NMR ($CDCl_3$) δ −56.9 (s, 3F); IR (neat) 2986, 1720, 1609, 1369, 1281 cm^{-1}; HRMS calcd. for $C_{18}H_{15}F_3O_2$: 321.1102 (M + H), found: 321.1103.

*4.2.4.7. (Z)-4,4,4-Trifluoro-1-(4-methoxyphenyl)-3-phenyl-2-butene (**5g-cis**).* Yield 62% (determined by ^{19}F NMR); ^{1}H NMR ($CDCl_3$) δ 3.71 (s, 2H), 3.78 (s, 3H), 6.13 (t, 1H, J = 7.95 Hz), 6.86 (d, 2H, J = 8.65 Hz), 7.15 (d, 2H, J = 8.55 Hz), 7.27–7.33 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 35.9, 55.3, 114.2, 117.2 (q, J = 33.7 Hz), 123.4 (q, J = 271.0 Hz), 126.9, 128.2, 128.5, 129.3, 131.4, 140.0, 140.6 (q, J = 3.1 Hz), 158.3; ^{19}F NMR ($CDCl_3$) δ −57.1 (s, 3F); IR (neat) 2910, 1651, 1512, 1494 cm^{-1}; HRMS calcd. for $C_{17}H_{15}F_3O$: 292.1075, found: 292.1081.

*4.2.4.8. (Z)-1-(4-Chlorophenyl)-2-(2-chlorophenyl)-3,3,3-trifluoropropene (**5h-cis**).* Yield 54%; ^{1}H NMR ($CDCl_3$) δ 6.90 (s, 1H), 7.31–7.41 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 122.5 (q, J = 275.0 Hz), 126.7, 128.6, 129.5 (q, J = 31.4 Hz), 129.8, 130.0, 130.1, 131.4, 132.3, 134.2, 134.9, 135.0, 139.7 (q, J = 3.8 Hz); ^{19}F NMR ($CDCl_3$) δ −57.7 (s, 3F); IR (neat) 2928, 1643, 1593, 1493 cm^{-1}. HRMS calcd. for $C_{15}H_9{}^{35}Cl_2F_3$: 316.0033, found: 316.0031.

*4.2.4.9. (Z)-1-(4-Chlorophenyl)-2-(3-chlorophenyl)-3,3,3-trifluoropropene (**5i-cis**).* Yield 94% (chromatographed on TLC plate); ^{1}H NMR ($CDCl_3$) δ 7.02 (s, 1H), 7.31–7.49 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 122.9 (q, J = 275.5 Hz), 126.4, 128.4, 128.5, 128.7, 129.7, 130.1, 131.2 (q, J = 30.3 Hz), 132.6, 134.4, 134.8, 137.8, 138.4 (q, J = 3.1 Hz); ^{19}F NMR ($CDCl_3$) δ −56.9 (s, 3F); IR (neat) 2927, 1643, 1593, 1492, 1377 cm^{-1}; HRMS calcd. for $C_{15}H_9{}^{35}Cl_2F_3$: 316.0033, found: 316.0031.

*4.2.4.10. (Z)-1,2-Bis(4-chlorophenyl)-3,3,3-trifluoropropene (**5j-cis**).* Yield 74%; ^{1}H NMR ($CDCl_3$) δ 6.99 (s, 1H), 7.32–7.39 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 123.0 (q, J = 275.6 Hz), 128.5, 128.7, 129.5, 129.97, 129.99, 131.3 (q, J = 31.1 Hz), 132.8, 134.7, 134.8, 137.9 (q, J = 2.6 Hz); ^{19}F NMR ($CDCl_3$) δ −57.0 (s, 3F); IR (neat) 2927, 1639, 1596, 1492, 1377 cm^{-1}; HRMS calcd. for $C_{15}H_9{}^{35}Cl_2F_3$: 316.0033, found: 316.0031.

*4.2.4.11. (Z)-1-(4-Chlorophenyl)-2-(4-methylphenyl)-3,3,3-trifluoropropene (**5k-cis**).* Yield 62%; mp 44–46 °C; ^{1}H NMR ($CDCl_3$) δ 2.37 (s, 3H), 7.00 (s, 1H), 7.18–7.23 (m, 2H), 7.21–7.37 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 123.3 (q, J = 275.8 Hz), 128.0, 128.4, 129.1, 129.98, 130.00, 132.6 (q, J = 30.5 Hz), 133.3, 134.3, 136.9 (q, J = 2.5 Hz), 138.6; ^{19}F NMR ($CDCl_3$) δ −56.9 (s, 3F); IR (KBr) 2924, 1643, 1593, 1489 cm^{-1}; HRMS calcd. for $C_{16}H_{12}{}^{35}ClF_3$: 296.0580, found: 296.0572.

*4.2.4.12. (Z)-1-(4-Chlorophenyl)-2-(4-methoxyphenyl)-3,3,3-trifluoropropene (**5l-cis**).* Yield 75%; mp 58–59 °C; ^{1}H NMR ($CDCl_3$) δ 3.85 (s, 3H), 6.90–6.98 (m, 3H), 7.20–7.41 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 55.3, 113.8, 123.3 (q, J = 276.0 Hz), 128.4, 128.5, 129.5, 130.0, 132.0 (q, J = 30.1 Hz), 133.4, 134.2, 136.4 (q, J = 3.6 Hz), 159.9; ^{19}F NMR ($CDCl_3$) δ −57.0 (s, 3F); IR (KBr) 2963, 1639, 1570, 1489 cm^{-1}; HRMS calcd. for $C_{16}H_{12}{}^{35}ClF_3O$: 312.0529, found: 312.0534.

*4.2.4.13. (Z)-1-(4-Chlorophenyl)-2-(4-nitrophenyl)-3,3,3-trifluoropropene (**5m-cis**).* Yield 59% (chromatographed on TLC plate); mp 73–76 °C; ^{1}H NMR ($CDCl_3$) δ 7.11 (s, 1H), 7.33–7.41 (m, 4H), 7.63 (d, J = 8.50 Hz, 2H), 8.28 (d, J = 9.00 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 122.4 (q, J = 276.6 Hz), 123.8, 128.7, 128.9, 129.1, 130.1, 131.1, 132.0, 134.4 (q, J = 36.1 Hz), 135.3, 139.8 (q, J = 3.4 Hz); ^{19}F NMR ($CDCl_3$) δ −56.7 (s, 3F); IR (KBr) 2933, 1668, 1512, 1442 cm^{-1}; HRMS calcd. for $C_{15}H_{10}{}^{35}ClF_3NO_2$: 328.0352 (M + H), found: 328.0357.

*4.2.4.14. (Z)-Ethyl 4-(1,1,1-trifluoro-3-(4-chlorophenyl)propen-2-yl)benzoate (**5n-cis**).* Yield 83% (chromatographed on TLC plate); mp 66–67 °C; ^{1}H NMR ($CDCl_3$) δ 1.41 (t, 3H, J = 7.25 Hz), 4.41 (d, 2H, J = 7.00 Hz), 7.06 (s, 1H), 7.32–7.40 (m, 4H), 7.52 (d, 2H, J = 8.00 Hz), 8.09 (d, 2H, J = 8.00 Hz); ^{13}C NMR ($CDCl_3$) δ 14.3, 61.2, 123.0 (q, J = 275.9 Hz), 128.1, 128.5, 129.7, 130.1, 130.6, 131.7 (q, J = 31.2 Hz), 132.6, 134.8, 138.5 (q, J = 3.0 Hz), 140.5, 166.0; ^{19}F NMR ($CDCl_3$) δ −56.9 (s, 3F); IR (KBr) 2963, 1635, 1562, 1492 cm^{-1}; HRMS calcd. for $C^{19}H_{15}{}^{35}ClF_3O_2$: 355.0713 (M + H), found: 355.0712.

*4.2.4.15. (Z)-1-(4-Chlorophenyl)-3,3-difluoro-2-phenyl-1-propene (**5o-cis**).* Yield 85% (chromatographed on TLC plate); ^{1}H NMR ($CDCl_3$) δ 6.57 (t, 1H, J = 54.41 Hz), 7.10 (s, 1H), 7.30 (d, 2H, J = 8.3 Hz), 7.38–7.43 (m, 5H), 7.58 (d, 2H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 112.9 (t, J = 236.2 Hz), 127.8, 128.36, 128.41, 128.9, 130.2, 132.9, 134.5, 135.4 (t, J = 9.9 Hz), 135.6, 135.9 (t, J = 21.9 Hz); ^{19}F NMR ($CDCl_3$) δ −111.0 (d, J = 54.2 Hz); IR (neat) 3030, 1593, 1490, 1388 cm^{-1}; HRMS calcd. for $C_{15}H_{11}{}^{35}ClF_2$: 264.0517, found: 264.0521.

*4.2.4.16. (Z)-1-(4-Chlorophenyl)-3,3,4,4,5,5-hexafluoro-2-phenyl-1-pentene (**5p-cis**).* Yield 80% (chromatographed on TLC plate); ^{1}H NMR ($CDCl_3$) δ 5.89 (tt, 1H, J = 52.31, 5.65 Hz), 7.41 (s, 1H), 7.22–7.50 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 107.8 (tt, J = 253.7, 30.9 Hz), 116.0 (tt, J = 253.7, 32.8 Hz), 128.1, 128.3, 128.6, 129.5, 131.8 (t, J = 19.9 Hz), 133.7, 133.9, 136.9 (t, J = 2.1 Hz), 141.1 (t, J = 4.1 Hz), 152.8 (t, J = 4.0 Hz); ^{19}F NMR ($CDCl_3$) δ −104.6 to −104.8 (m, 2F), −127.5 to −128.0 (m, 2F), −136.7 to −138.0 (m, 2F); IR (neat) 1492, 1400, 1137, 1091 cm^{-1}; HRMS calcd. for $C_{17}H_{11}{}^{35}ClF_6$: 364.0453, found: 364.0455.

References

[1] (a) D. O'Hagen, H.S. Rzepa, Chem. Commun. (1997) 645–652;
(b) J.T. Welch, Tetrahedron 43 (1987) 3123–3197;
(c) J. Mann, Chem. Soc. Rev. 16 (1987) 381–436.
[2] (a) M. Prakesch, D. Grée, S. Chandrasekhar, R. Grée, Eur. J. Org. Chem. (2005) 1211–1232;
(b) K. Mikami, Y. Itoh, M. Yamanaka, Chem. Rev. 104 (2004) 1–16;
(c) R.P. Singh, J.M. Shreeve, Tetrahedron 56 (2000) 7613–7632;
(d) G.K.S. Prakash, A.K. Yudin, Chem. Rev. 97 (1997) 757–786;

(e) J.H. Steenis, A. Gen, J. Chem. Soc. Perkin Trans. 1 (2002) 2117–2133;
(f) M.A. McClinton, D.A. McClinton, Tetrahedron 48 (1992) 6555–6666;
(g) I. Ojima, Chem. Rev. 88 (1988) 1011–1030.

[3] (a) T. Konno, T. Daitoh, A. Noiri, J. Chae, T. Ishihara, T. Mantani, Org. Lett. 6 (2004) 933–936;
(b) G. Németh, R. Kapiller-Dezsøofi, G. Lax, G. Simig, Tetrahedron 52 (1996) 12821–12830;
(c) G. ÁbraHám, T. Horváth, L. Toldy, J. Borvendég, E. Csányi, É. Kiss, I. Hermann-Szente, K. Tory (Gyógyszerkuntató Intézet), Hungarian Patent 17853 (1979).
(d) G. ÁbraHám, T. Horváth, L. Toldy, J. Borvendég, E. Csányi, É. Kiss, I. Hermann-Szente, K. Tory, Drugs Fut. 10 (1985) 395;
(e) G. ÁbraHám, T. Horváth, L. Toldy, J. Borvendég, E. Csányi, É. Kiss, I. Hermann-Szente, K. Tory, Drugs Fut. 11 (1986) 426;
(f) G. ÁbraHám, T. Horváth, L. Toldy, J. Borvendég, E. Csányi, É. Kiss, I. Hermann-Szente, K. Tory, Drugs Fut. 12 (1987) 497;
(g) G. ÁbraHám, T. Horváth, L. Toldy, J. Borvendég, E. Csányi, É. Kiss, I. Hermann-Szente, K. Tory, Drugs Fut. 13 (1988) 480.

[4] (a) M. Shimizu, T. Fujimoto, H. Minezaki, Takeshi, Hata, T. Hiyama, J. Am. Chem. Soc. 123 (2001) 6947–6948;
(b) M.P. Jennings, E.A. Cork, V. Ramachandran, J. Org. Chem. 65 (2000) 8763–8766;
(c) S. Peng, F.-L. Qing, Y. Guo, Synlett (1998) 859–860;
(d) F.-L. Qing, W.-Z. Gao, J. Ying, J. Org. Chem. 65 (2000) 2003–2006;
(e) J. Thibonnet, G. Prié, M. Abarbri, A. Duchêne, J.-L. Parrain, Tetrahedron Lett. 40 (1999) 3151–3154;
(f) T.E. Nickson, J. Org. Chem. 53 (1988) 3870–3872.

[5] (a) N. Miyaura, A. Suzuki, Chem. Rev. 95 (1995) 2457–2483;
(b) J.K. Stille, Angew. Chem. Int. Ed. Engl. 25 (1986) 508–524;
(c) M.A.J. Duncton, G. Pattenden, J. Chem. Soc. Perkin Trans. 1 (1999) 1235–1246;
(d) E. Shirakawa, K. Yamasaki, T. Hiyama, Synthesis (1998) 1544–1549;
(e) T.N. Mitchell, Synthesis (1992) 803–815;
(f) E. Negishi, Acc. Chem. Res. 15 (1982) 340–348.

[6] (a) J. Chae, T. Konno, M. Kanda, T. Ishihara, H. Yamanaka, J. Fluorine Chem. 120 (2003) 185–193;
(b) Y. Hanzawa, K. Kawagoe, N. Tanahashi, Y. Kobayashi, Tetrahedron Lett. 25 (1984) 4749–4752.

[7] (a) J.J. Eisch, in: B.M. Trost, I. Fleming (Eds.), Comprehensive Organic Synthesis, vol. 8, Pergamon Press, Oxford, 1991, p. 733;
(b) K. Maruoka, H. Sano, K. Shinoda, S. Nakai, H. Yamamoto, J. Am. Chem. Soc. 108 (1986) 6036.

[8] (a) T. Konno, J. Chae, M. Kanda, G. Nagai, K. Tamura, T. Ishihara, H. Yamanaka, Tetrahedron 59 (2003) 7571–7580;
(b) T. Hiyama, K. Sato, M. Fujita, Bull. Chem. Soc. Jpn. 62 (1989) 1352–1354;
(c) N. Yoneda, S. Matsuoka, N. Miyaura, Bull. Chem. Soc. Jpn. 63 (1990) 2124–2126;
(d) J.E. Bunch, C.L. Bumgardner, J. Fluorine Chem. 36 (1987) 313–317;
(e) A.J. Laurent, I.M. Le Drean, A. Selmi, Tetrahedron Lett. 32 (1991) 3071–3074;
(f) B.C. Hamper, J. Org. Chem. 53 (1988) 5558;
(g) Y. Kobayashi, T. Yamashita, K. Takahashi, H. Kuroda, I. Kumadaki, Tetrahedron Lett. 23 (1982) 343–344.

[9] (a) M.F. Semmelhack, R.D. Stauffer, A. Yamashita, J. Org. Chem. 42 (1977) 3180–3188;
(b) M.F. Semmelhack, R.D. Stauffer, J. Org. Chem. 40 (1975) 3619–3621.

[10] (a) I. Beletskaya, A. Pelter, Tetrahedron 53 (1997) 4957–5026;
(b) K. Burgess, M.J. Ohlmeyer, Chem. Rev. 91 (1991) 1179–1191;
(c) H. Nöth, D. Männig, Angew. Chem. Int. Ed. Engl. 24 (1985) 878.