Available online at www.sciencedirect.com
ScienceDirect
Journal of Fluorine Chemistry 128 (2007) 1158–1167
www.elsevier.com/locate/fluor

Hydrodefluorinations by low-valent niobium catalyst

Kohei Fuchibe, Yoshitaka Ohshima, Ken Mitomi, Takahiko Akiyama *

Department of Chemistry, Faculty of Science, Gakushuin University, 1-5-1 Mejiro, Toshima-ku, Tokyo 171-8588, Japan

Received 18 April 2007; received in revised form 6 June 2007; accepted 7 June 2007

Abstract

Catalytic hydrodefluorinations of organofluorine compounds by low-valent niobium catalyst were developed. In the presence of niobium(V) chloride (typically, 5 mol%), fluorobenzenes, α,α,α-trifluorotoluenes and (trifluoromethyl)pyridines were hydrodefluorinated with lithium aluminum hydride to give the corresponding benzenes, toluenes and methylpyridines in good yields, respectively.

Keywords: C–F bond activation; Catalysis; Fluorobenzene; Hydrodefluorination; Niobium; Reduction; Trifluoromethylpyridine; Trifluorotoluene

1. Introduction

The carbon–fluorine bond is one of the strongest single bonds found in organic molecules [1]. Essentially because of the high bond dissociation energies, the synthetic utility of organofluorine compounds is limited and transition metal catalyzed C–F bond activations have not been realized until recently [2–4].

The hydrodefluorination of organofluorine compounds is an important C–F bond activation [5] because it provides a way to destroy fluorine-containing atmospheric pollutants [6] such as CFCs (ozone-depleting materials) [7] and perfluoroalkanes (greenhouse gases) [8]. The reductive detoxification of such gaseous compounds having quite long half-lives in the atmosphere [3c] is a practical way to reduce the levels of fluorous, environmental hazardous wastes [9].

In spite of its importance, catalytic hydrodefluorination emerged only in the last decade (Scheme 1). Aizenberg and Milstein were the first to report catalytic hydrodefluorination of hexafluorobenzene (rhodium, in 1994) [10,11]. Kiplinger and Richmond reported the zirconocene(IV)-mediated reduction of octafluoronaphthalene [12]. In the early stage of hydrodefluorination chemistry, reactions of perfluorobenzene derivatives were mainly studied because these compounds are highly electron-deficient and are therefore relatively reactive [13]. In recent years, however, the catalytic hydrodefluorination of non-activated fluorobenzenes has been developed. Young and Grushin reported the rhodium-catalyzed hydrodefluorination of fluoronaphthalenes [14]. Jones and co-workers reported the zirconocene(IV)-mediated hydrodefluorination of fluorobenzene and fluoroalkanes [15]. Other catalytic reactions that involve the use of late transition metal catalysts have been reported by Fort and co-workers [16] and others [17]. The hydrodefluorination of fluoroalkenes has been also reported recently [18,19].

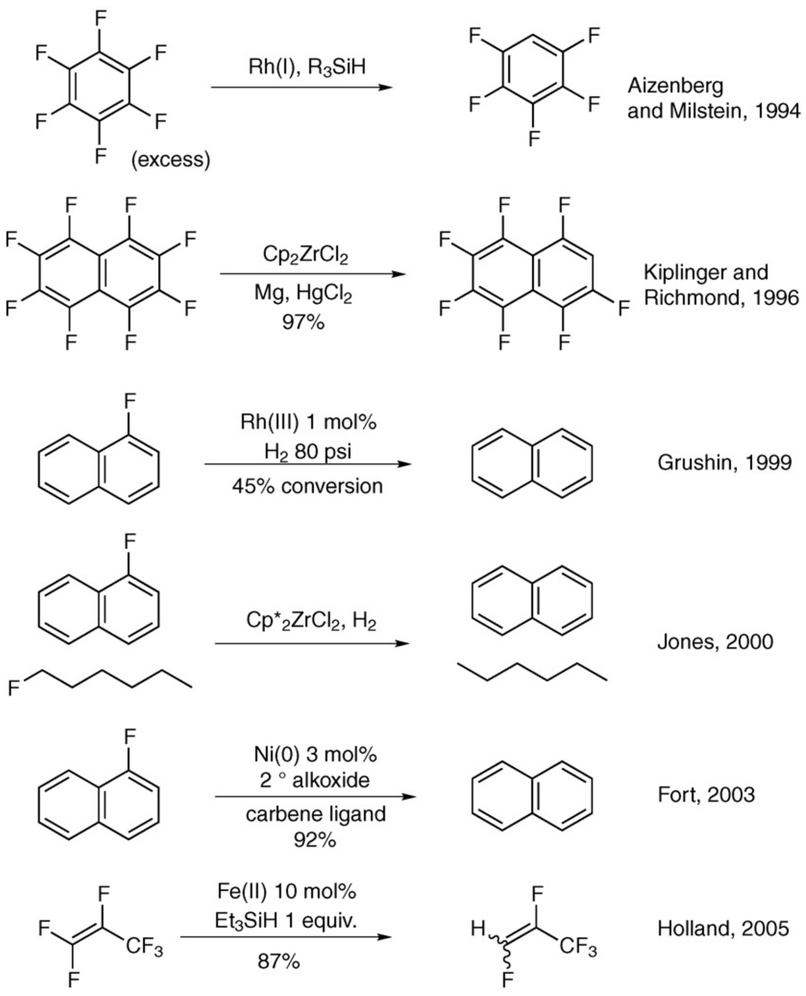
In this study, we focused on the hydrodefluorination of organofluorine compounds with early transition metal catalysts. In terms of Pauling's electronegativity, fluorine is the most electronegative element in the periodic table ($EN_{(F)} = 3.98$). On the other hand, early transition metal elements are more electropositive than late transition metal elements (for instance, $EN_{(Nb)} = 1.6$ and $EN_{(Pd)} = 2.2$). We expected that the electrostatic interaction of fluorine with an early transition metal center is responsible for the high catalytic activity.

Based on the above considerations, we examined catalytic hydrodefluorination with early transition metal catalysts and found that low-valent niobium species, which is generated from niobium(V) chloride and lithium aluminum hydride in situ, is an efficient catalyst. The synthetic utility of niobium, mainly in the +III form, was pioneered by Pedersen and co-workers in the mid 1980s [20–22], and the chemistry of Lewis acid niobium(V) has been investigated in recent years [21a,23]. We disclose herein the novel catalytic activity of niobium at a low oxidation state in the hydrodefluorination of fluorobenzenes [24], α,α,α-trifluorotoluenes [25] and (trifluoromethyl)pyridines [26].

---

* Corresponding author. Tel.: +81 3 3986 0221; fax: +81 3 5992 1029.
E-mail address: takahiko.akiyama@gakushuin.ac.jp (T. Akiyama).

0022-1139/$ – see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.jfluchem.2007.06.003



Scheme 1.

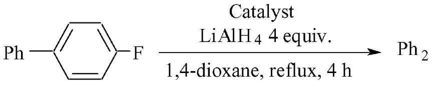
2. Results and discussion

2.1. Reaction conditions

The catalytic activities of various early and late transition metal salts were examined by using 4-fluorobiphenyl **1a** as substrate (Table 1). A 1,4-dioxane solution of **1a** was treated with lithium aluminum hydride (4 equiv.) in the presence of 20 mol% of a metal salt at room temperature. After refluxing for 4 h, the reaction was quenched with water. Among the metal salts examined, niobium(V) chloride gave the highest yield of biphenyl **2a** (entries 1–6, 10–13). It is worth noting that palladium and nickel chloride gave essentially similar results to that of the control experiment (entries 12–14). The load of niobium(V) chloride could be reduced to 5 mol% (entries 6–9).

The low-valent niobium-catalyzed hydrodefluorination of **1a** was found to proceed smoothly in ethereal solvents (Table 2): **2a** was obtained in good yields in 1,4-dioxane or DME (entries 1 and 2). When the reaction was performed at 60 °C, the yield of **2a** decreased to 52% (entry 3). The yield of **2a** also decreased when the reaction was carried out in THF (entry 4). In toluene or hexane, **2a** was obtained in low yields

Table 1
Survey on catalyst



1a **2a**

Entry	Catalyst, mol%	**2a** (%)	Recovery of **1a** (%)
1	$ZrCl_4$, 20	63	35
2	VCl_3, 20	54	37
3	$TaBr_5$, 20	56	29
4	$TaCl_5$, 20	60	34
5	$NbBr_5$, 20	60	26
6	$NbCl_5$, 20	94	0
7	$NbCl_5$, 10	93	0
8	$NbCl_5$, 5	94	0
9	$NbCl_5$, 2	41	47
10	WCl_6, 20	0	97
11	$FeCl_3$, 20	64	29
12	$PdCl_2$, 20	26	73
13	$NiCl_2$, 20	27	72
14	None	28	57

Table 2
Effect of solvents and reducing agents[a]

Entry	Solvent	Reducing agent	**2a** (%)	Recovery of **1a** (%)
1	1,4-dioxane	$LiAlH_4$	94	0
2	DME	$LiAlH_4$	91	0
3[b]	DME	$LiAlH_4$	52	42
4	THF	$LiAlH_4$	73	18
5	Toluene	$LiAlH_4$	10	82
6[c]	Hexane	$LiAlH_4$	7	90
7	DME	DIBAL	0	90
8	DME	$NaBH_4$	0	89
9	DME	n-Bu_3SnH	0	92
10	DME	Et_3SiH	0	92
11	DME	Nb turnings[d]	0	93

DME = 1,2-Dimethoxyethane.

[a] *Conditions*: **1a**, $NbCl_5$ 5 mol%, $LiAlH_4$ 2 equiv., reflux, 4 h.

[b] The reaction was performed at 60 °C.

[c] $NbCl_5$ 10 mol%.

[d] $LiAlH_4$ was not used. The reaction was performed for 7 h.

(entries 5 and 6). Although the coordination of solvent molecule(s) to niobium seems to play an important role in the C–F bond activation, the solubility of lithium aluminum hydride in ethereal solvent is also likely an important factor. Based on the yield and the temperature, we chose DME as the most suitable solvent.

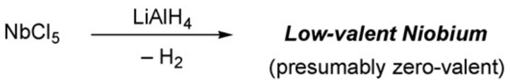
Lithium aluminum hydride was found to be the most efficient reducing agent. Use of DIBAL, sodium borohydride, tributyltin hydride and triethylsilane resulted in recovery of starting material **1a** (entries 7–10). Niobium turnings, in the absence of lithium aluminum hydride, also did not give **1a** (entry 11).

When lithium aluminum hydride was added to the dioxane solution of **1a** and niobium(V) chloride at room temperature, the clear yellow solution instantaneously became colorless and turned dark gray exothermically. The resulting heterogeneous mixture violently evolved gas upon heating [27]. It has been reported that niobium(V) chloride is reduced with lithium aluminum hydride in diethyl ether at 0 °C to give metallic niobium and dihydrogen [28]. We believe that zero-valent, metallic niobium is generated in the reaction medium (Scheme 2). In this manuscript, however, we use the term 'low-valent niobium' because we have not succeeded in detecting zero-valent niobium directly. Here, it should be stated that Oshima and Sato reported reductive reactions under the niobium(V) chloride/sodium aluminum hydride system in 1982 [29,30].

2.2. Catalytic hydrodefluorination of fluorobenzenes

2.2.1. Hydrodefluorination of fluorobenzene derivatives

Low-valent niobium was found to be quite effective for the hydrodefluorination of monofluorobenzenes (Table 3) [24]. *o*-, *m*- and *p*-Fluorobiphenyls **1a–c** were reduced in the optimized system to give biphenyl **2a** in good yields (entries 1, 2 and 4). Not only electronically neutral fluorobiphenyls but also electron-rich fluorobiphenyls were reduced readily to give the corresponding products (entries 5–8). It is noteworthy that the methyl ether moiety of **1g** was tolerant to the reaction conditions (entry 8). Arai and Nishida reported facile ether cleavage of methyl ethers by niobium(V) chloride [31]. The low-valent niobium catalyst was found to be less Lewis acidic than the niobium(V). Carbon–chlorine bonds and carbon–bromine bonds of **1h** and **1i** were reduced prior to the carbon-fluorine bonds (entries 9 and 11). The complete reduction of these fluorobenzenes was also accomplished by prolonging the reaction (entries 10 and 12). 1-Fluoronaphthalene gave naphthalene in satisfactory yield (entry 13). 3,4,5-Trifluorobiphenyl **1k** was reduced completely to give biphenyl **2a** in high yield (entry 14). **1k** selectively gave 3,5-difluorobiphenyl **2g** when the reaction was quenched within 15 min (entry 15).



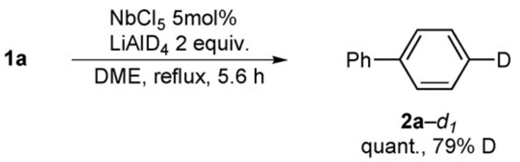
Scheme 2.

As is described in Section 1, perfluorobenzene derivatives are relatively reactive and the catalytic hydrodefluorination of the perfluorobenzenes was extensively studied [10,12,18a]. In contrast, the catalytic hydrodefluorination of non-activated fluorobenzene derivatives is fairly limited [14,16,17]. Table 3 suggests that low-valent niobium species is a highly active and useful catalyst for the hydrodefluorination of monofluorobenzenes.

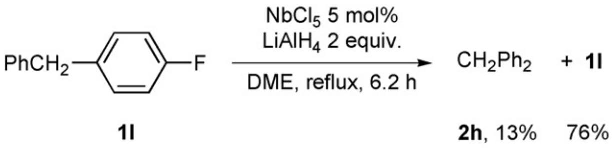
2.2.2. Mechanistic considerations

It was found that the hydrogen introduced into the product originates from lithium aluminum hydride (Scheme 3). Hydrodefluorination of **1a** with lithium aluminum deuteride gave 4-deuteriobiphenyl (**2a**-d_1) in quantitative yield. The deuterium incorporation was determined to be 79% D based on the integrals on the ^1H NMR spectrum.

Conjugation of the substrates strongly affected the rate of the reaction. Hydrodefluorination of benzyl(fluoro)benzene **1l** did not proceed smoothly and only 13% yield of corresponding hydrocarbon **2h** was obtained (Scheme 4). Further, *p*- and *o*-phenylated fluorobenzenes reacted faster than the corresponding *m*-isomer; *p*- and *o*-fluorobiphenyls **1a** and **1c** gave **2a** in high yields within 4 h (Table 3, entries 1 and 4), whereas the hydrodefluorination of *m*-fluorobiphenyl **1b** required 6 h (entries 2 and 3). **1k** underwent para-selective hydrodefluorination after a short time (entry 15).



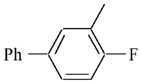
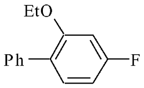
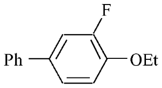
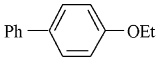
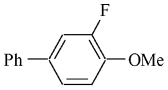
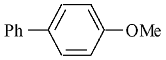
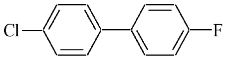
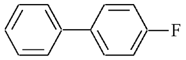
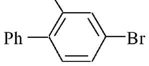
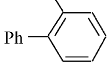
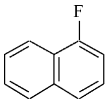
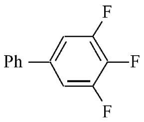
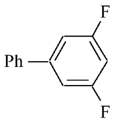
Scheme 3.



Scheme 4.

Table 3
Catalytic hydrodefluorination of fluorobenzenes

$$\text{Ar–F} \xrightarrow[\text{DME, reflux}]{\text{NbCl}_5\text{ 5 mol\%, LiAlH}_4\text{ 2 equiv.}} \text{Ar–H}$$

Entry	Fluorobenzene	Time (h)	Product	Yield (%)	Recovery (%)
1	4-Fluorobiphenyl (**1a**)	4.0	Biphenyl (**2a**)	91	0
2	3-Fluorobiphenyl (**1b**)	6.0	**2a**	91	0
3	**1b**	4.0	**2a**	64	34
4	2-Fluorobiphenyl (**1c**)	4.0	**2a**	93	0
5	 (**1d**)	10.0	3-Phenyltoluene (**2b**)	90	0
6	 (**1e**)	10.2	2-Ethoxybiphenyl (**2c**)	Quant.	0
7	 (**1f**)	8.0	 (**2d**)	90	0
8	 (**1g**)	4.0	 (**2e**)	87[a]	0
9	 (**1h**)	0.6	 (**1a**)	19[b]	76
10	**1h**	4.0[c]	**2a**	98[d]	0
11	 (**1i**)	0.5	 (**1c**)	40	49
12	**1i**	8.0[e]	**2a**	90	0
13	 (**1j**)	2.2	Naphthalene (**2f**)	81	0
14	 (**1k**)	6.0[e]	**2a**	91	0
15	**1k**	0.25[f]	 (**2g**)	80[g]	6

[a] 5% yield of 4-phenylphenol was obtained.
[b] Biphenyl **2a** was not isolated.
[c] 3.5 equiv. of $LiAlH_4$ was used.
[d] 4-Fluorobiphenyl **1a** was not isolated.
[e] 10 mol% of $NbCl_5$ and 6 equiv. of $LiAlH_4$ were used.
[f] 6 equiv. of $LiAlH_4$ was used.
[g] Biphenyl **2a** was not obtained. A few percents yield of *m*-hydrodefluorinated product was detected by GC–MS analysis.

Based on the observations, we propose an S_NAr-like, nucleophilic substitution mechanism of the fluorine atom with metal hydride species. The pendant phenyl group stabilizes the anionic charge formed in the addition intermediate by delocalization. Phenyl groups on *p*- and *o*-positions, in particular, stabilize the partial anionic charge efficiently [15b,32].

2.3. Catalytic hydrodefluorination of α,α,α-trifluorotoluenes

2.3.1. Hydrodefluorination of α,α,α-trifluorotoluenes

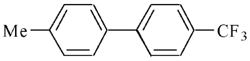
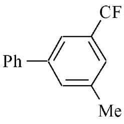
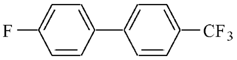
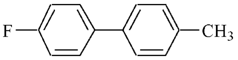
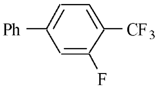
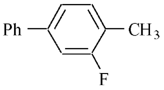
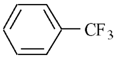
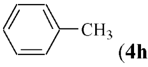
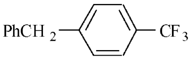
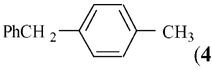
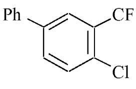
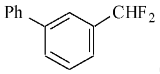
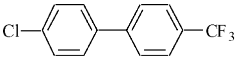
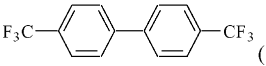
It is well recognized that the CF_3 groups of α,α,α-trifluorotoluenes are considerably stable and remain intact under vigorous conditions. The C–F bonds are indeed benzylic, but chemical transformation of the C–F bonds is extremely difficult [33]. Hydrodefluorination of the trifluorotoluenes was accomplished only very recently [34].

The low-valent niobium catalyst was found to be applicable to the hydrodefluorination of α,α,α-trifluorotoluene derivatives (Table 4) [25]. Under conditions identical to those described in Table 3, phenyl trifluorotoluenes **3a–f** gave the corresponding toluenes in high yields (entries 1–6). It is noteworthy that the aromatic C–F bonds were not hydrodefluorinated under the reaction conditions (entries 5 and 6). In the case of 2-phenyl-α,α,α-trifluorotoluene **3g**, corresponding 2-phenyltoluene **4g** was obtained but in 51% yield, and fluorene **5** was obtained in 15% yield (entry 7). **5** was generated by double activation of the C–F bond and the aromatic C–H bond [26a]. Not only phenyl trifluorotoluenes but also parent and benzyl trifluorotoluenes **3h** and **3i** gave corresponding products **4h** and **4i**, respectively (entries 8 and 9). When chlorotrifluorotoluene **3j** was subjected to the reaction conditions, both C–F bonds and the C–Cl bond were reduced to give *m*-phenyltoluene **2b** in 81% yield (entry 10). When the reduction of **3j** was performed with a reduced amount of lithium aluminum hydride (6 versus 3 equiv.), partial reduction products **3b** and **6**, in which no chlorine atom survived, were obtained (entry 11). On the other hand, chlorotrifluorotoluene **3k** gave considerable amounts of chlorotoluene **4j** (entry 12). Reactivities of the CF_3 group, the aromatic C–F bond, and the aromatic C–Cl bond were thus found to follow roughly the order $C_{Ar}–F < C_{Ar}–Cl \sim ArCF_3$. The reduction of 4,4′-bis(trifluoromethyl)biphenyl **3l** also proceeded smoothly to give **4c** in 58% yield (entry 13).

2.3.2. *Partial reduction of bis(trifluoromethyl)benzene*

The selective, stepwise hydrodefluorination of bis(trifluoromethyl)benzene **3m** was also accomplished (Scheme 5). With a large excess of lithium aluminum hydride, **3m** gave completely hydrodefluorinated product **4d** in 78% yield. In contrast, **3m** gave partially hydrodefluorinated product **3d** in

Table 4
Catalytic hydrodefluorination of α,α,α-trifluorotoluenes[a]

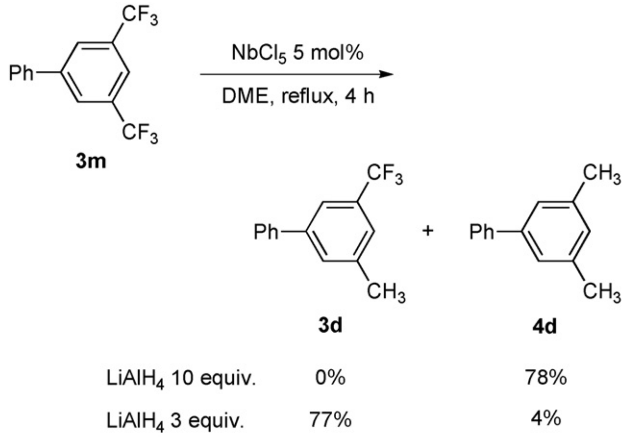
Entry	Trifluorotoluene	Time (h)	$LiAlH_4$ (equiv.)	Products, yields (%)
1	4-Phenyl-α,α,α-trifluorotoluene (**3a**)	4.0	4	4-Phenyltoluene (**4a**), 96
2	3-Phenyl-α,α,α-trifluorotoluene (**3b**)	6.9	4	3-Phenyltoluene (**2b**), 94
3	 (**3c**)	4.0	5	4,4′-Dimethylbiphenyl (**4c**), 85
4	 (**3d**)	4.0	5	3,5-Dimethylbiphenyl (**4d**), 82
5	 (**3e**)	4.0 4.0	5 3	 (**4e**), 82
6	 (**3f**)			 (**4f**), quant.
7	2-Phenyl-α,α,α-trifluorotoluene (**3g**)	4.3	4	2-Phenyltoluene (**4g**), 51 Fluorene (**5**), 15
8	 (**3h**)	8.0	4	 (**4h**), quant.[b]
9[c]	 (**3i**)	8.0	10	 (**4i**), 58
10	 (**3j**)	4.0	6	**2b**, 81
11	**3j**	4.0	3	**2b**, 33, **3b**, 12,  (**6**), 27
12	 (**3k**)	4.0	4	4-Chloro-4′-methylbiphenyl (**4j**), 38 **4a**, 41
13	 (**3l**)	4.0	10	**4c**, 58

---

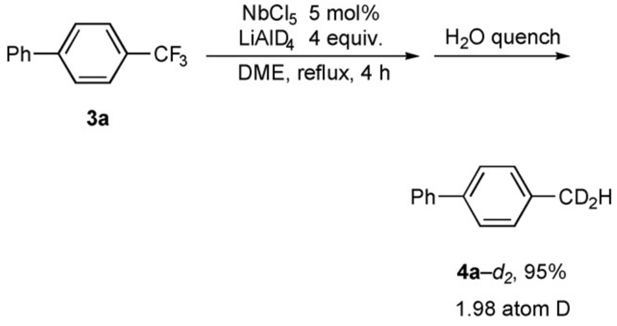
[a] *Conditions*: $NbCl_5$ 5 mol%, DME (1,2-dimethoxyethane), reflux.

[b] NMR yield after distillation. Dibromomethane was used as an internal standard.

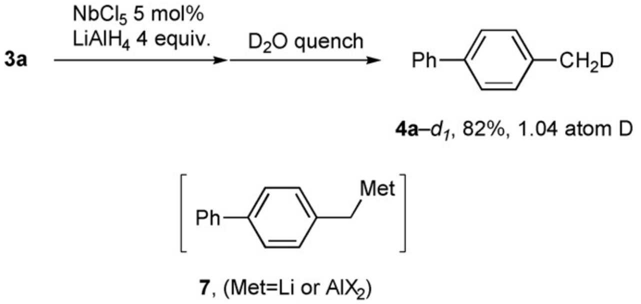
[c] $NbCl_5$ 100 mol%.



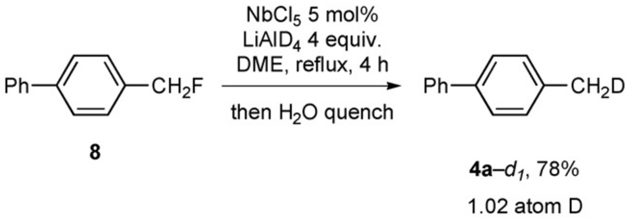
Scheme 5.



Scheme 6.



Scheme 7.



Scheme 8.

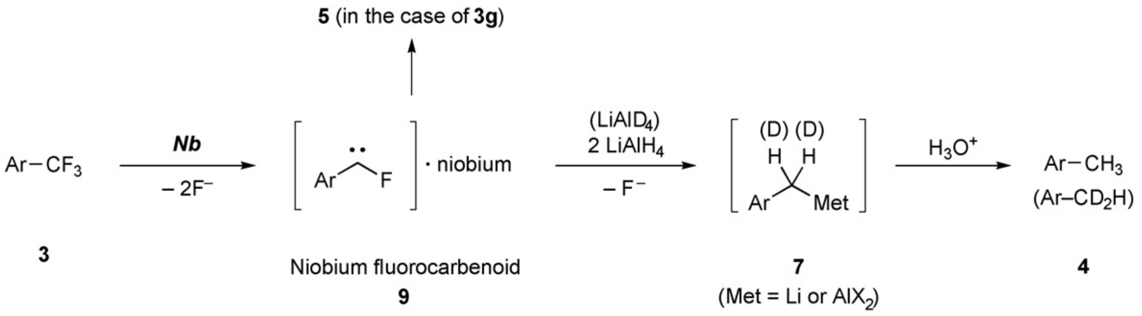
77% yield with 3 equiv. of the reducing agent. One of the most general methods to prepare α,α,α-trifluorotoluene derivatives is the fluorine–chlorine exchange of α,α,α-trichlorotoluenes [35], which are prepared by chlorination of the corresponding toluenes [36]. The low-valent niobium-catalyzed partial reduction is a potentially useful method to produce aromatic compounds that possess both CH_3 and CF_3 groups.

2.3.3. Mechanistic considerations

Deuterium labeling experiments suggested that the niobium-catalyzed hydrodefluorination of α,α,α-trifluorotoluenes does not proceed via a simple S_N2 mechanism; hydrodefluorination of **3a** with lithium aluminum deuteride gave 4-phenyl-α,α-dideuteriotoluene **4a**-d_2 (95% yield, 1.98 atom D, Scheme 6). On the other hand, when the reaction was quenched with deuterium oxide, 4-phenyl-α-deuteriotoluene **4a**-d_1 was obtained (82% yield, 1.04 atom D, Scheme 7). Apparently, two of the fluorines are replaced with hydride hydrogens in situ, and (dihydro)benzylic anion equivalent **7** is formed [37].

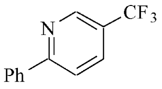
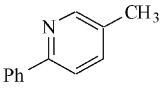
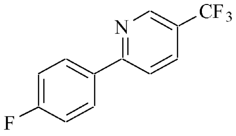
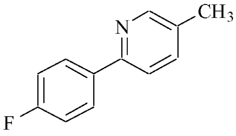
The precursor of **7** was found *not* to be benzyl fluoride **8** (Scheme 8). Separately prepared **8** was treated with lithium aluminum deuteride, and the reaction was quenched with H_2O. We found that deuterium was incorporated into the product (**4a**-d_1, 1.02 atom D). This result suggests that **8** is not involved in the hydrodefluorination of **3a**.

The results of the deuterium labeling experiments and the formation of fluorene **5** can be explained by assuming a niobium fluorocarbenoid intermediate (Scheme 9). Fluorocarbenoid species **9** is reductively generated from substrate **3** and low-valent niobium species. **9** absorbs two hydride anions from the reducing agent and liberates one fluoride anion to produce benzylanion equivalent **7**. Protonation of **7** affords toluene derivative **4**. On the other hand, when *o*-phenyltrifluorotoluene **3g** is used, **9** undergoes formal carbene insertion into the neighboring aromatic C–H bond to give **5** (double activation)



Scheme 9.

Table 5
Hydrodefluorination of (tifluromethyl)pyridine[a]

Entry	(Trifluoromethyl)pyridine	Time (h)	Products, yields (%)
1	 (**10a**)	4	 65 (**11a**)
2[b]	**10a**	4	Complex mixture
3	 (**10b**)	0.5	 40 (**11b**), 4, **11a**
4	**10b**	6.5[c]	**11b**, 9, **11a**, 41

[a] *Conditions*: (trifluoromethyl)pyridine, $NbCl_5$ 20 mol%, $LiAlH_4$ 4 equiv., 1,4–dioxane, reflux.
[b] $NbCl_5$ was not used.
[c] 4 equiv. of $LiAlH_4$, 4 h then 2 equiv. of $LiAlH_4$, 2.5 h.

[26a]. However, we do not have solid data to support the formation of intermediate **9** at present.

2.4. Hydrodefluorination of (trifluoromethyl)pyridines

The hydrodefluorination of (trifluoromethyl)pyridine derivatives was also performed. The low-valent niobium catalyst exhibited remarkable effects in this system: 2-phenyl-5-(trifluoromethyl)pyridine **10a** underwent smooth hydrodefluorination with 20 mol% of the niobium catalyst in dioxane (Table 5, entry 1) [38]. In contrast, **10a** gave a complex mixture in the absence of the catalyst (entry 2). GC–MS analysis suggested that the pyridine nucleus was competitively reduced in the latter case. Fluoro(trifluoromethyl)pyridine **10b** underwent CF_3-selective hydrodefluorination to give corresponding fluoro(methyl)pyridine **11b** in good yield (entry 3). Complete hydrodefluorination of **10b** also proceeded to give **11a** after prolonged reaction with an excess amount of the reducing agent (entry 4).

3. Conclusions

Low-valent niobium was found to be an efficient catalyst for the hydrodefluorination of fluorobenzenes, α,α,α-trifluorotoluenes and (trifluoromethyl)pyridines. Using 5 mol% low-valent niobium catalyst, high yields of the corresponding hydrocarbons were obtained. Although the chemistry of group 5 metal elements is underdeveloped compared to that of late transition metal elements, the results described herein strongly demonstrate the synthetic utility of group 5 metals as catalysts.

4. Experimental

4.1. General information

NMR spectra were recorded on Unity Inova-400 instrument (Varian Ltd., 400 MHz for ^1H, 100 MHz for ^{13}C, 376 MHz for ^{19}F) using $CDCl_3$ as a solvent. Chemical shifts (δ) for ^1H were referenced to tetramethylsilane ($\delta = 0.00$ ppm) as an internal standard. Chemical shifts (δ) for ^{13}C were referenced to a solvent signal ($CDCl_3$, $\delta = 77.0$ ppm). Chemical shifts (δ) for ^{19}F were referenced to α,α,α-trifluorotoluene ($\delta = -63.9$ ppm) as an internal standard. IR spectra were recorded on FTIR-8600PC instrument (Shimadzu Co.) using $CHCl_3$ as a solvent. Mass spectra (LRMS) were recorded on GCMS-QP5000 instrument (Shimadzu Co.).

4.2. Typical procedures

Caution: Addition of solid lithium aluminum hydride to niobium(V) chloride must be carried out with great care. The reaction mixture possibly flow out of the container due to the exothermic, violent gas evolution.

4.2.1. Hydrodefluorination of fluorobenzenes

Reaction of 4-fluorobiphenyl **1a** is described as a typical procedure (Table 3, entry 1); to a DME solution (3 mL) of *p*-fluorobiphenyl (217 mg, 1.26 mmol) and $NbCl_5$ (17 mg, 0.06 mmol) was added $LiAlH_4$ (96 mg, 2.52 mmol) in one portion. The clear yellow solution turned dark gray immediately and gas evolved exothermically. After being refluxed for 4 h, the reaction mixture was quenched with H_2O at 0 °C. Sodium tartrate (0.2 g) was added and extraction with ethyl acetate gave the crude mixture. Purification by silica gel column chromatography (hexane) afforded biphenyl **2a** (176 mg, 1.14 mmol, 91%).

4.2.2. Hydrodefluorination of α,α,α-trifluorotoluenes

Reduction of **3a** is described as a typical procedure (Table 4, entry 1): to a DME solution (5 mL) of **3a** (308 mg, 1.39 mmol) and $NbCl_5$ (18 mg, 0.068 mmol) was added solid lithium aluminum hydride (208 mg, 5.47 mmol) carefully. The mixture was magnetically stirred and allowed to reflux for 4 h. The reaction was quenched with water at 0 °C and a small amount of sodium tartrate (ca. 200 mg) was added for the ease of extraction. Products were extracted with ethyl acetate three times and the combined organic layers were dried over anhydrous sodium sulfate. The organic solvents were removed under reduced pressure and purification by column chromatography (SiO_2, hexane) gave **4a** (218 mg, 1.33 mmol, 96% yield) as a colorless crystal.

*4.2.3. Complete hydrodefluorination of 3,5-bis(trifluoromethyl)biphenyl **3m** (Scheme 5)*

To a DME solution (9.4 mL) of **3m** (225 mg, 0.778 mmol) and $NbCl_5$ (11 mg, 0.039 mmol) was added solid lithium aluminum hydride (295 mg, 7.78 mmol) carefully. The mixture was magnetically stirred and allowed to reflux for 4 h. The reaction was quenched with water at 0 °C and a small amount of sodium tartrate (ca. 200 mg) was added for the ease of extraction. Products were extracted with ethyl acetate three times and the combined organic layers were dried over anhydrous sodium sulfate. The organic solvents were removed under reduced pressure and purification by column chromatography (SiO_2, hexane) gave **4d** (111 mg, 0.607 mmol, 78% yield) and 3-difluoromethyl-5-methylbiphenyl (5 mg, 0.02 mmol, 3% yield).

*4.2.4. Partial hydrodefluorination **3m** (Scheme 5)*

To a DME solution of **3m** (1.23 g, 4.25 mmol) and $NbCl_5$ (58 mg, 0.22 mmol) was added solid lithium aluminum hydride (477 mg, 12.6 mmol) carefully. The mixture was magnetically stirred and allowed to reflux for 4 h. The reaction was quenched with water at 0 °C and a small amount of sodium tartrate (ca. 500 mg) was added for the ease of extraction. Products were extracted with ethyl acetate three times and the combined organic layers were dried over anhydrous sodium sulfate. The organic solvents were removed under reduced pressure and purification by column chromatography (SiO_2, hexane) gave **3d** (773 mg, 3.27 mmol, 77% yield), **4d** (31 mg, 0.17 mmol, 4%, yield), and a mixture of 3,5-bis(difluoromethyl)biphenyl and 3-difluoromethyl-5-methylbiphenyl (105 mg, 2% and 9% yields, respectively).

4.2.5. Hydrodefluorination of (trifluoromethyl)pyridines

Reaction of 5-trifluoromethyl-2-phenylpyridine **10a** is described as a typical procedure (Table 5, entry 1). To a 1,4-dioxane solution of **10a** (273 mg, 1.23 mmol) and $NbCl_5$ (66 mg, 0.24 mmol) was added solid lithium aluminum hydride (188 mg, 4.95 mmol) carefully. The mixture was magnetically stirred and allowed to reflux for 4 h. The reaction was quenched with water at 0 °C and a small amount of sodium tartrate (ca. 200 mg) was added for the ease of extraction. Products were extracted with ethyl acetate three times and the combined organic layers were dried over anhydrous sodium sulfate. The organic solvents were removed under reduced pressure and purification by column chromatography (SiO_2, hexane/ethyl acetate = 10/1) gave **11a** (133 mg, 0.79 mmol, 65% yield) as a colorless crystal.

4.3. Characterization of the products

4.3.1. Hydrodefluorination products of fluorobenzenes

^1H NMR spectra of **2a** [39], **2b** [40], **2d** [41], **2e** [42], **1a** [43], **1c** [44], **2f** [45] and **2h** [46] were in complete agreement with those in the literature.

*4.3.1.1. 2-Ethoxybiphenyl (**2c**).* ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.37$ (3H, t, $J = 6.8$ Hz), 4.06 (2H, q, $J = 6.8$ Hz), 6.99 (1H, d, $J = 8.0$ Hz), 7.04 (1H. dt, $J = 7.6$ 1.2 Hz), 7.29–7.38 (3H, m), 7.42 (2H, t, $J = 8.0$ Hz), 7.60 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.7$, 63.9, 112.6, 120.8, 126.7, 127.8, 128.5, 129.5, 130.8, 130.9, 138.6, 155.8. IR ($CHCl_3$): $\tilde{\nu} = 3020$, 1475, 1435, 1209, 1126, 1045, 928, 731, 671 cm^{-1}. LRMS (70 eV, EI): m/z (rel. int.) = 115 (61), 169 (98, M^+-Et), 170 (100, M^+-Et+H), 198 (58, M^+).

*4.3.1.2. 3,5-Difluorobiphenyl (**2g**).* ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.78$ (1H, tt, $J = 8.8$, 2.0 Hz), 7.10 (2H, dd, $J = 8.8$, 2.4 Hz), 7.39 (1H, t, $J = 7.2$ Hz), 7.45 (2H, t, $J = 7.2$ Hz), 7.54 (2H, d, $J = 7.2$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 102.4$ (t, $J = 100$ Hz), 109.9 (dd, $J = 18$, 7 Hz), 127.0, 128.4, 129.0, 138.9, 144.5 (t, $J = 10$ Hz), 163.3 (dd, $J = 247$, 13 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -110.95$ to -111.06 (m). IR ($CHCl_3$): $\tilde{\nu} = 1620$, 1601, 1421, 1340, 1119, 989, 860, 696 cm^{-1}. LRMS (70 eV, EI): m/z (rel. int.) = 170 (13, M^+-HF), 190 (100, M^+).

4.3.2. Hydrodefluorination products of α,α,α-trifluorotoluenes

Characterization data of **4a**, **4c–f**, **4i**, **3b** and **6** were described in our previous communication [25]. Characterization of **4g** and **5** was described in our previous communication [26a]. ^1H NMR spectrum of **4h** was in complete agreement with the authentic toluene.

*4.3.2.1. 4-Chloro-4′-methylbiphenyl (**4j**).* ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.39$ (3H, s), 7.25 (2H, d, $J = 8.0$ Hz), 7.38 (2H, d, $J = 8.0$ Hz), 7.45 (2H, d, $J = 8.0$ Hz), 7.50 (2H, d, $J = 8.0$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.1$, 126.8, 128.2, 128.8, 129.6, 133.0, 137.1, 137.4, 139.6. IR ($CHCl_3$): $\tilde{\nu} = 2926$, 2855, 1489, 1481, 1096, 1007, 810 cm^{-1}. LRMS (70 eV, EI): m/z (rel. int.) = 167 (55, M^+-Cl), 202 (100, $M^+(C_{13}H_{11}{}^{35}Cl^+)$), 204 (33, $M^+(C_{13}H_{11}{}^{37}Cl^+)$).

4.3.3. Hydrodefluorination products of (trifluoromethyl)pyridines

*4.3.3.1. 5-Methyl-2-phenylpyridine (**11a**).* ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.38$ (3H, s), 7.39 (1H, t, $J = 7.2$ Hz), 7.46 (2H, t, $J = 7.2$ Hz), 7.56 (1H, dd, $J = 8.0$, 2.0 Hz), 7.63 (1H, d, $J = 8.0$ Hz), 7.96 (2H, dd, $J = 8.4$, 1.2 Hz), 8.52 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 18.1$, 120.0, 126.7, 128.6, 128.7, 131.6, 137.3, 139.4, 150.0, 154.8. IR ($CHCl_3$): $\tilde{\nu} = 3020$, 1479, 1213, 752, 667 cm^{-1}. LRMS (70 eV, EI): m/z (rel. int.) = 169 (100, M^+), 168 (53, M^+-H), 154 (9, M^+-CH_3).

*4.3.3.2. 2-(4-Fluorophenyl)-5-methylpyridine (**11b**).* ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.37$ (3H, s), 7.14 (2H, t, $J = 8.8$ Hz), 7.54–7.58 (2H, m), 7.94 (2H, dd, $J = 9.2$, 5.2 Hz), 8.50 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 18.1$, 115.5 (d, $J = 21.3$ Hz), 119.7, 128.4 (d, $J = 8.4$ Hz), 131.5, 135.6, 137.4, 150.0, 153.8, 163.2 (d, $J = 246$ Hz). ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -115.0$ to -114.9 (m). IR ($CHCl_3$): $\tilde{\nu} = 1605$, 1514, 1479, 1157, 826 cm^{-1}. LRMS (70 eV, EI): *m/z* (rel. int.) = 187 (100, M^+), 186 (42, M^+−H).

Acknowledgements

This work was supported in part by Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology, Japan (No. 18750036). This work was also supported by Saneyoshi scholarship foundation (No. 1818).

References

[1] S.J. Blanksby, G.B. Ellison, Acc. Chem. Res. 36 (2003) 255–263.

[2] (a) T. Schaub, M. Backes, U. Radius, J. Am. Chem. Soc. 128 (2006) 15964–15965;
(b) A. Steffen, M.I. Sladek, T. Braun, B. Neumann, H.-G. Stammler, Organometallics 24 (2005) 4057–4064;
(c) J. Terao, A. Ikumi, H. Kuniyasu, N. Kambe, J. Am. Chem. Soc. 125 (2003) 5646–5647;
(d) N. Yoshikai, H. Mashima, E. Nakamura, J. Am. Chem. Soc. 127 (2005) 17978–17979;
(e) T. Saeki, Y. Takashima, K. Tamao, Synletters (2005) 1771–1774;
(f) M. Fujiwara, J. Ichikawa, T. Okauchi, T. Minami, Tetrahedron Lett. 40 (1999) 7261–7265;
(g) Y. Ishii, N. Chatani, S. Yorimitsu, S. Murai, Chem. Lett. (1998) 157–158;
(h) Y.M. Kim, S. Yu, J. Am. Chem. Soc. 125 (2003) 1696–1697;
(i) See also: Y. Kiso, K. Tamao, M. Kumada, J. Organomet. Chem. 50 (1973) C12–C14.

[3] For reviews, see:
(a) T.G. Richmond, Activation of unreactive bonds and organic synthesis, in: S. Murai (Ed.), Topics in Organometallic Chemistry, vol. 3, Springer, Berlin, 1999, pp. 243–269;
(b) J.L. Kiplinger, T.G. Richmond, C.E. Osterberg, Chem. Rev. 94 (1994) 373–431;
(c) J. Burdeniuc, B. Jedlicka, R.H. Crabtree, Chem. Ber. 130 (1997) 145–154.

[4] See also:
(a) S.A. Begum, J. Terao, N. Kambe, Chem. Lett. 36 (2007) 196–197;
(b) K. Hirano, K. Fujita, H. Yorimitsu, H. Shinokubo, K. Oshima, Tetrahedron Lett. 45 (2004) 2555–2557.

[5] O. Paleta, Replacement of fluorine by hydrogen, in: B. Baasner, H. Hagemann, J.C. Tatlow (Eds.), Organo-Fluorine Compounds/Methods of Organic Chemistry, vol. E 10b/Part 2, Houben-Weyl, Stuttgart, 2000, pp. 306–344.

[6] F. Alonso, I.P. Beletskaya, M. Yus, Chem. Rev. 102 (2002) 4009–4138.

[7] M.J. Molina, F.S. Rowland, Nature 249 (1974) 810–812.

[8] (a) D.G. Victor, G.J. MacDonald, Climat. Change 42 (1999) 633–662;
(b) C.M. Roehl, D. Boglu, C. Brühl, G.K. Moortgat, Geophys. Res. Lett. 22 (1995) 815–818;
(c) P.L. Timms, J. Chem. Soc., Dalton Trans. (1999) 815–822.

[9] Commodore Chemical Co. in Columbus Ohio developed reductive disposals of CFCs.

[10] (a) M. Aizenberg, D. Milstein, Science 265 (1994) 359–361;
(b) M. Aizenberg, D. Milstein, J. Am. Chem. Soc. 117 (1995) 8674–8675.

[11] See also: T. Imamoto, T. Takeyama, T. Kusumoto, Chem. Lett. (1985) 1491–1492.

[12] (a) J.L. Kiplinger, T.G. Richmond, Chem. Commun. (1996) 1115–1116;
(b) J.L. Kiplinger, T.G. Richmond, J. Am. Chem. Soc. 118 (1996) 1805–1806.

[13] See also:
(a) B.L. Edelbach, W.D. Jones, J. Am. Chem. Soc. 119 (1997) 7734–7742;
(b) N.A. Jasim, R.N. Perutz, A.C. Whitwood, T. Braun, J. Izundu, B. Neumann, S. Rothfeld, H.-G. Stammler, Organometallics 23 (2004) 6140–6149.

[14] R.J. Young Jr., V.V. Grushin, Organometallics 18 (1999) 294–296.

[15] (a) B.M. Kraft, R.J. Lachicotte, W.D. Jones, J. Am. Chem. Soc. 122 (2000) 8559–8560;
(b) B.M. Kraft, R.J. Lachicotte, W.D. Jones, J. Am. Chem. Soc. 123 (2001) 10973–10979;
(c) W.D. Jones, Dalton Trans. (2003) 3991–3995.

[16] S. Kuhl, R. Schneider, Y. Fort, Adv. Synth. Catal. 345 (2003) 341–344.

[17] (a) H. Yang, H. Gao, R.J. Angelici, Organometallics 18 (1999) 2285–2287;
(b) P.P. Cellier, J.-F. Spindler, M. Taillefer, H.-J. Cristau, Tetrahedron Lett. 44 (2003) 7191–7195.

[18] (a) J. Vela, J.M. Smith, Y. Yu, N.A. Ketterer, C.J. Flaschenriem, R.J. Lachicotte, P.L. Holland, J. Am. Chem. Soc. 127 (2005) 7857–7870;
(b) B.M. Kraft, W.D. Jones, J. Am. Chem. Soc. 124 (2002) 8681–8689;
(c) M.S. Kirkham, M.F. Mahon, M.K. Whittlesey, Chem. Commun. (2001) 813–814;
(d) D. Noveski, T. Braun, M. Schulte, B. Neumann, H.-G. Stammler, Dalton Trans. (2003) 4075–4083;
(e) E. Clot, C. Mégret, B.M. Kraft, O. Eisenstein, W.D. Jones, J. Am. Chem. Soc. 126 (2004) 5647–5653.

[19] See also: D. Guijarro, P. Martínez, M. Yus, Tetrahedron, 59 (2003) 1237–1244.

[20] (a) E.J. Roskamp, S.F. Pedersen, J. Am. Chem. Soc. 109 (1987) 6551–6553;
(b) J.B. Hartung, S.F. Pedersen, Oganometallics 9 (1990) 1414–1417.

[21] For reviews:
(a) C.K.Z. Andrade, Curr. Org. Synth. 1 (2004) 333–353;
(b) J.A. Labinger, in: G. Wilkinson, F.G.A. Stone, E.W. Abel (Eds.), Comprehensive Organometallic Chemistry, vol. 3, Pergamon Press, New York, 1982, pp. 705–782;
(c) D.E. Wigley, S.D. Gray, in: E.W. Abel, F.G.A. Stone, G. Wilkinson (Eds.), Comprehensive organometallic Chemistry II, vol. 5, Pergamon, New York, 1995, pp. 57–153.

[22] See also:
(a) Y. Kataoka, K. Takai, K. Oshima, K. Utimoto, Tetrahedron Lett. 31 (1990) 365–368;
(b) Y. Kataoka, J. Miyai, M. Tezuka, K. Takai, K. Oshima, K. Utimoto, Tetrahedron Lett. 31 (1990) 369–372;
(c) S. Arai, S. Takita, A. Nishida, Eur. J. Org. Chem. (2005) 5262–5267;
(d) Y. Obora, M. Kimura, M. Tokunaga, Y. Tsuji, Chem. Commun. (2005) 901–902;
(e) J. Szymoniak, J. Besançon, C. Moïse, Tetrahedron 50 (1994) 2841–2848;
(f) B. Kammermeier, G. Beck, D. Jocobi, H. Jendralla, Angew. Chem. Int. Ed. Engl. 33 (1994) 685–687;
(g) A.C. Williams, P. Sheffels, D. Sheehan, T. Livinghouse, Organometallics 8 (1989) 1566–1567.

[23] (a) S. Kobayashi, K. Arai, H. Shimizu, Y. Ihori, H. Ishitani, Y. Yamashita, Angew. Chem. Int. Ed. 44 (2005) 761–764;
(b) K. Arai, M.M. Salter, Y. Yamashita, S. Kobayashi, Angew. Chem. Int. Ed. 46 (2007) 955–957.

[24] K. Fuchibe, T. Akiyama, Synletters (2004) 1282–1284.

[25] K. Fuchibe, Y. Ohshima, K. Mitomi, T. Akiyama, Org. Lett. 9 (2007) 1497–1499.

[26] See for our preliminary C–C bond forming reactions using CF_3 groups, also:
(a) K. Fuchibe, T. Akiyama, J. Am. Chem. Soc. 128 (2006) 1434–1435;
(b) K. Fuchibe, K. Mitomi, T. Akiyama, Chem. Lett. 36 (2007) 24–25.

[27] Dihydrogen was detected by gas indicator (GASTEC corporation, gas indicator tube No. 30).

[28] M.E. Kost, A.I. Golovanova, Zh. Neorg. Khim. 22 (1977) 977–979.

[29] M. Sato, K. Oshima, Chem. Lett. (1982) 157–160.

[30] Other reductive reactions by (transition) metal/lithium aluminum hydride systems:

(a) J.O. Osby, S.W. Heinzman, B. Ganem, J. Am. Chem. Soc. 108 (1986) 67–72;
(b) E.C. Ashby, J.J. Lin, J. Org. Chem. 43 (1978) 1263–1265;
and reference [11].
[31] (a) See also: Y. Sudo, S. Arai, A. Nishida, Eur. J. Org. Chem. (2006) 752–758;
(b) Q. Guo, T. Miyaji, R. Hara, B. Shen, T. Takahashi, Tetrahedron 58 (2002) 7327–7334.
[32] B.M. Kraft, W.D. Jones, J. Organomet. Chem. 658 (2002) 132–140.
[33] (a) C. Saboureau, M. Troupel, S. Sibille, J. Périchon, J. Chem. Soc. Chem. Commun. (1989) 1138–1139;
(b) D. Ferraris, C. Cox, R. Anand, T. Lectka, J. Am. Chem. Soc. 119 (1997) 4319–4320;
(c) H. Amii, Y. Hatamoto, M. Seo, K. Uneyama, J. Org. Chem. 66 (2001) 7216–7218;
See also:
(d) K. Uneyama, H. Amii, J. Fluorine Chem. 114 (2002) 127–131.
[34] V.J. Scott, R. Çelenligil-Çetin, O.V. Ozerov, J. Am. Chem. Soc. 127 (2005) 2852–2853.
[35] (a) J.H. Simons, C.J. Lewis, J. Am. Chem. Soc. 60 (1938) 492–1492;
(b) A.J. Bloodworth, K.J. Bowyer, J.C. Mitchell, Tetrahedron Lett. 28 (1987) 5347–5350.
[36] (a) P.G. Harvey, F. Smith, M. Stacey, J.C. Tatlow, J. Appl. Chem. 4 (1954) 319–325;
(b) F.D. Marsh, W.B. Farnham, D.J. Sam, B.E. Smart, J. Am. Chem. Soc. 104 (1982) 4680–4682.
[37] It was confirmed that **7** was not generated by deprotonation of the product. Treatment of isolated **4a** under the reaction conditions and quenching the reaction with deuterium oxide did not afford deuterionated **4a** at all (88% recovery).
[38] When the reaction was performed in DME 57% yield of **11a** was obtained.
[39] C.P. Pouchert, J. Behnke (Eds.), The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra, Edition I, vol. 2, Aldrich Chemical Company, Inc., 1993, p. 28.
[40] C.P. Pouchert, J. Behnke (Eds.), I ed., The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra, vol. 2, Aldrich Chemical Company, Inc., 1993, p. 32.
[41] N.H. Lajis, M.N. Khan, H.A. Hassan, Tetrahedron 49 (1993) 3405–3410.
[42] C.P. Pouchert, J. Behnke (Eds.), I ed., The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra, vol. 2, Aldrich Chemical Company, Inc., 1993, p. 216.
[43] C.P. Pouchert, J. Behnke (Eds.), I ed., The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra, vol. 2, Aldrich Chemical Company, Inc., 1993, p. 157.
[44] C.P. Pouchert, J. Behnke (Eds.), I ed., The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra, vol. 2, Aldrich Chemical Company, Inc., 1993 , p. 156.
[45] C.P. Pouchert, J. Behnke (Eds.), I ed., The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra, vol. 2, Aldrich Chemical Company, Inc., 1993, p. 40.
[46] C.P. Pouchert, J. Behnke (Eds.), I ed., The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra, vol. 2, Aldrich Chemical Company, Inc., 1993, p. 7.