

Synthesis of Trifluoromethyl Ketones by Palladium-Catalyzed Cross-Coupling Reaction of Phenyl Trifluoroacetate with Organoboron Compounds

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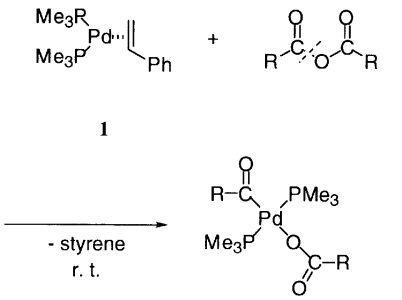
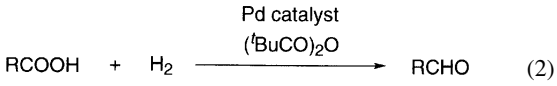
Cross-coupling reaction of aryl trifluoroacetates with organoboron compounds catalyzed by palladium complexes gives trifluoromethyl ketones in moderate to excellent yields under mild conditions. The catalytic process has been designed on the basis of fundamental studies dealing with oxidative addition of phenyl trifluoroacetate to a Pd(0) complex to give a (phenoxo)(trifluoroacetyl)palladium(II) complex and its subsequent reaction with phenylboronic acid to liberate phenyl trifluoromethyl ketone. The catalytic cycle is proposed to be composed of (a) oxidative addition of the ester to give acyl(aryloxo)palladium intermediate, (b) the subsequent transmetallation with arylboron compounds, and (c) reductive elimination. Palladium(0) complexes, as well as catalysts prepared in situ from palladium acetate and 3 molar amounts of tributylphosphine or phosphite at room temperature, serve as convenient and effective catalysts. The process is applicable to a wide range of phenyl- and naphthylboronic acids to give various aryl trifluoromethyl ketones under mild conditions. Aryl perfluoroalkyl ketone derivatives can be similarly prepared in high yields from various phenyl perfluoroalkanecarboxylates and arylboronic acids.

Cleavage of carbon-halogen bonds in organic halides promoted by transition metal complexes, notably by palladium complexes, has been extensively used in catalytic processes.[1] In contrast, cleavage of carbon–oxygen bonds in oxygen-containing organic compounds by transition metal complexes has not been well exploited, except for the processes using allylic esters.[2] In our attempts to find new transition-metal-catalyzed synthetic processes, we have been concerned with studies of fundamental processes of the carbon-oxygen bond cleavage in oxygen-containing organic compounds promoted by low valent transition metal complexes.[3,4,5] Our recent study revealed that the C–O bonds in carboxylic anhydrides can be readily cleaved on interaction with a Pd(0) complex **1** (Eq. 1).[4]



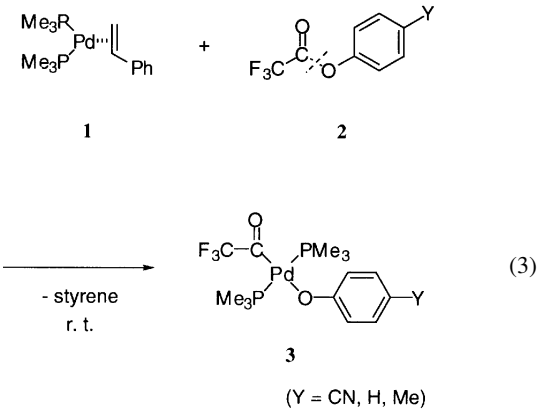
(1)

Based on the fundamental studies on cleavage of the C–O bonds in acid anhydrides on interaction with Pd(0) complexes, we have developed novel catalytic hydrogenation processes to convert a variety of carboxylic anhydrides[4b] and carboxylic acids[6] into corresponding aldehydes under mild conditions (Eq. 2).



(2)

Another type of C–O bond cleavage process of potential utility in organic synthesis is the C–O bond cleavage of carboxylic esters. Recently, we reported that a palladium(0) complex having basic and compact trimethylphosphine ligands reacted with aryl trifluoroacetates **2** under mild conditions to cause the C–O bond cleavage between the acyl and the OAr groups to give *trans*-(aryloxo)(trifluoroacetyl)bis(trimethylphosphine)palladium(II) **3** (Eq. 3).[5]

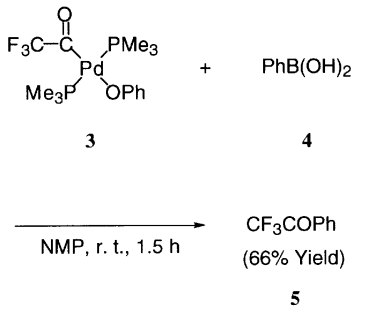


(3)

If the oxidative addition process involving the acyl-aryloxy bond cleavage in carboxylic esters can be combined with other elementary processes such as transmetallation, olefin insertion, and reductive elimination, we can anticipate development of useful catalytic processes. The present paper is concerned with the transmetallation of the acyl-aryloxy type complexes with arylboron compounds and the application of the basic information derived thereof to synthesis of aryl fluoroalkyl ketones catalyzed by palladium complexes.

Results and Discussion

Reaction of *trans*-(Phenoxo)(trifluoroacetyl)bis(trimethylphosphine)-palladium(II) 3 with Phenylboronic Acid. We first examined the possibility to replace the phenoxo ligand in the *trans*-(phenoxo)(trifluoroacetyl)bis(trimethylphosphine)palladium **3** generated by the acyl-OPh bond cleavage in phenyl trifluoroacetate on interaction with the Pd(0) complex.[5] In fact, we found that treatment of **3** with phenylboronic acid **4** at room temperature yielded phenyl trifluoromethyl ketone **5** in a good yield (Eq. 4). The result suggests that the transmetallation of **3** with **4** takes place readily to give a (phenyl)(trifluoroacetyl)palladium intermediate that further releases ketone **5** rapidly on reductive elimination.

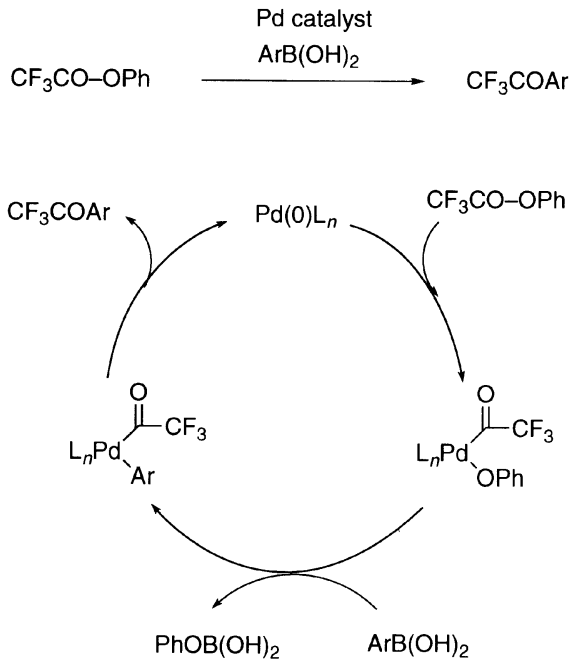


3 **4** **5** (4)

On the basis of the result, we designed a catalytic cycle, shown in Scheme 1, to convert the aryl trifluoroacetates into trifluoromethyl ketones by combining the C-O bond cleavage with transmetallation in a manner similar to the Suzuki–Miyaura coupling process where the carbon–halogen cleavage is involved.[7,8]

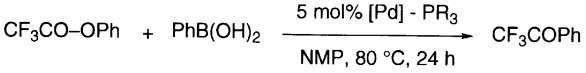
Trimethylphosphine is known to serve as an excellent ligand to prepare the phosphine-coordinated model compounds, but it is often not suitable for the real catalytic process. Therefore, we examined the catalytic processes using other tertiary phosphine ligands.

Catalytic Process Converting Various Phenyl Perfluoroalkanecarboxylates into Aryl Perfluoroalkyl Ketones on Interaction with Arylboron Compounds Catalyzed by Palladium Complexes. (1) Effect of Catalyst. The catalytic cross-coupling process of phenyl trifluoroacetate with phenylboronic acid was found to proceed in the presence of zerovalent palladium complexes such as $[Pd(dba)_2]$ (dba = dibenzylideneacetone) in combination with tributylphosphine in nitrogen-containing polar solvents at 80 °C to afford phenyl trifluoromethyl ketone. Table 1 summarizes the effect of the catalysts employed for the reaction.



Scheme 1. Catalytic cycle for the formation of trifluoromethyl ketones.

Table 1. Effect of Catalysts on the Cross-Coupling Reaction of Phenyl Trifluoroacetate with Phenylboronic Acid



Run	Pd-catalyst		Yield/%[a)]
1	$[Pd(dba)_2]$		0
2		+ 2P^{n}Bu$_3$	38
3		+ 3P^{n}Bu$_3$	53
4		+ 4P^{n}Bu$_3$	36
5		+ DPPP	9
6		+ DPPB	40
7	$[Pd(PPh_3)_4]$		trace
8	$[Pd(OAc)_2]$		0
9		+ 2P^{n}Bu$_3$	61
10		+ 3P^{n}Bu$_3$	82
11		+ 4P^{n}Bu$_3$	70
12		+ 2P(O^{n}Bu)$_3$	51
13		+ 3P(O^{n}Bu)$_3$	76
14		+ 2PCy$_3$	33
15		+ 3PCy$_3$	20
16		+ 2PPh$_3$	16
17		+ 3PPh$_3$	20
18	Pd/C		0

a) Determined by GC using $^nC_{14}H_{30}$ as an internal standard.

Whereas the $[Pd(dba)_2]$ complex alone proved to be inactive, addition of tributylphosphine gave good yields of the ketone. Addition of three equivalents of P(^{n}Bu)$_3$ per palladium developed a good yield. Increase in the amount of the tributylphos-

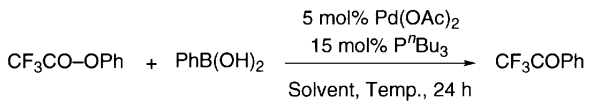
phine further to four equivalents caused a slight decrease in the ketone yield. Employment of a bidentate ditertiary phosphine ligand such as 1,2-bis(diphenylphosphino)propane (DPPP) was not suitable, whereas the ditertiary phosphine ligands such as 1,2-bis(diphenylphosphino)butane (DPPB) that form a larger and more flexible chelate ring with the palladium center gave a moderate yield of the ketone. These results suggest that the role of the tertiary phosphine ligand is to stabilize and control the reactivity of the palladium center, but use of excess of the monotertiary phosphine ligand or of a chelate ligand that strongly binds to palladium should be avoided. The reason why [$Pd(PPh_3)_4$] was not so effective may be due to coordination of excess PPh_3 ligands to hinder the catalytic process.

These results indicate that a Pd(0) complex serves as a catalyst and suggest that the catalytic cycle is composed of some processes between Pd(0) and Pd(II) species. However, in a real system it is not necessary to use the palladium(0) complex, but instead the mixed system of $Pd(OAc)_2$ in combination with a suitable ligand can be more convenient. It is known that the palladium(II) acetate is reduced to a Pd(0) complex in a solution with formation of phosphine oxide mediated by water.[9] The results shown in Table 1 indicate that $Pd(OAc)_2$ used as the catalyst precursor in combination with tributylphosphine or tributyl phosphite serves as a good and convenient catalyst in synthesis. Again, addition of an excess of the ligand had a deteriorating effect. Employment of more bulky tricyclohexylphosphine was less effective than use of tributylphosphine. Addition of triphenylphosphine was not suitable. Palladium on carbon was found ineffective as the catalyst.

(2) Effects of Solvents and Temperature. Table 2 compares the reactions in various solvents in the presence of $Pd(OAc)_2$–$3P^nBu_3$ system. In 1-methyl-2-pyrrolidinone (NMP), the yield of the phenyl trifluoromethyl ketone increased on raising the reaction temperature from room temperature to 60 and to 80 °C, whereas further increase to 100 °C had a deteriorating effect.

Solvents used in the cross-coupling reaction had a considerable influence on the yields of phenyl trifluoromethyl ketone.

Table 2. Effect of Solvent and Temperature on the Cross-Coupling Reaction of Phenyl Trifluoroacetate with Phenylboronic Acid



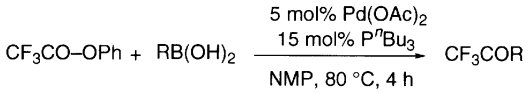
Run	Temp/°C	Solvent	Yield/%[a)]
1	r. t.	NMP	0
2	60	NMP	33
3	80	NMP	82
4	100	NMP	73
5	80	dioxane	trace
6	80	toluene	0
7	80	CH_3CN	trace
8	80	CMF	63

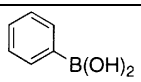
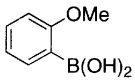
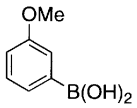
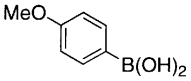
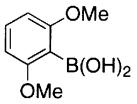
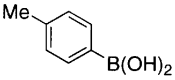
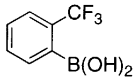
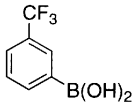
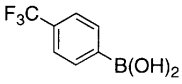
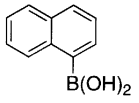
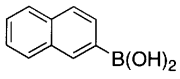
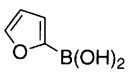
a) Determined by GC using $^nC_{14}H_{30}$ as an internal standard.

Higher yields can be obtained in polar solvents such as *N*,*N*-dimethylformamide (DMF) and NMP than in less polar solvents like dioxane and toluene, while acetonitrile was not effective.

(3) Scope and Limitation. Table 3 shows the applicability of the process to substituted phenylboronic acids containing various substituents at ortho-, meta-, and para-positions. Substitution with the methoxy group at the ortho position gave a

Table 3. Synthesis of Trifluoromethyl Ketones via the Palladium-Catalyzed Cross-Coupling of Phenyl Trifluoroacetate with Arylboronic Acids



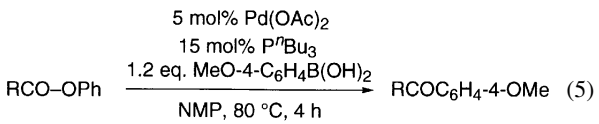
Run	Boronic acid	Yield/%[a),b)]
1		81[a)]
2		68[b)]
3		78[b)]
4		84[b)]
5		0[a)]
6		74[b)]
7		0[a)]
8		66[a)]
9		17[a)]
10		66[b)]
11		72[b)]
12		0[a)]

a) Determined by GC using $^nC_{14}H_{30}$ as an internal standard.
b) Isolated yield

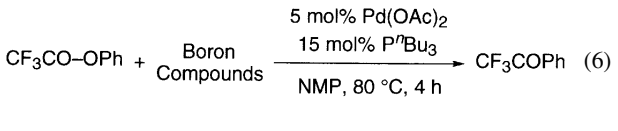
somewhat lower yield, but the substituent such as methoxy and methyl group at meta or para position gave good yields (Run 2–4, 6). Substitution with the two methoxy groups at ortho positions completely hindered the catalytic process, indicating the steric hindrance of the two adjacent substituents (Run 5).[10]

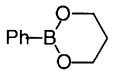
Substitution with an electron-withdrawing group such as trifluoromethyl group at the ortho position of phenylboronic acid gave no ketone (Run 7), whereas substitution of the trifluoromethyl group at the para position produced the corresponding ketone in a poor yield (Run 9). On the other hand, the electron-withdrawing substituent at the meta position gave a good yield of ketone (Run 8). Other arylboronic acids such as 1-naphthyl- and 2-naphthylboronic acids afforded the ketones in moderate yields (Run 10 and 11), whereas 2-furylboronic acid yielded no ketone (Run 12).

The palladium-promoted coupling process is applicable to other phenyl perfluoroalkanecarboxylates. The synthesis with a protocol similar to the one employed for phenyl trifluoroacetate gave perfluoroalkyl ketones in good yields, starting from phenyl pentafluoropropionate and heptafluorobutyrate (Eq. 5).



Organoboron compounds other than arylboronic acids were also examined. Employment of sodium tetraphenylborate in a quantity somewhat higher than equimolar amount in combination with the phenyl trifluoroacetate gave phenyl trifluoromethyl ketone in 59%. On the other hand, reduction in the amount of the tetraphenyl borate to one-fourth caused a drop in the yield down to 20%, suggesting that only a part of the four phenyl groups in $NaBPh_4$ is available for the transfer. Other phenylboron compounds such as Bu_4NBPh_4 and 2-phenyl-1,3,2-dioxaborinane were ineffective (Eq. 6).



Boron Compounds		
	$NaBPh_4$	59%
	Bu_4NBPh_4	0%
		0%

The main features of the catalytic processes are consistent with a catalytic cycle composed of the elementary processes shown in Scheme 1. Although the palladium-catalyzed cross-coupling reaction of organic halides with organoboron compounds generally requires the assistance of a base,[7] no base is required in the present reaction of phenyl trifluoroacetates with arylboronic acids giving some advantage to the present system for synthesizing compounds less tolerant to the presence of a base.

In the Suzuki–Miyaura coupling of aryl- and alkenyl halides with aryl- and alkenylboronic acids or esters, addition of a base such as NaOEt, KOAc, and NaOH is necessary to drive the reactions. The effect of addition of these bases was accounted for as replacement of the halide ligand in the catalyst intermediate with the alkoxide, carboxylate, or hydroxide that are more susceptible to the transmetallation with the oxophilic arylboronic acids or esters than a halide. In the present case, on the other hand, use of phenyl trifluoroacetate gives the (phenoxo)(trifluroacetyl)palladium intermediate having the phenoxide ligand suitable for the direct transmetallation process with the oxophilic arylboronic acid.[11]

Conclusion

On the basis of fundamental studies on oxidative addition of phenyl trifluoroacetate with a Pd(0) complex to give the (phenoxo)(trifluoroacetyl)palladium type complex and its subsequent transmetallation process, we could devise a novel type of catalytic process to convert aryl perfluoroalkanecarboxylates and organoboron compounds into aryl perflluoroalkyl ketones without using a base. Since suitable processes of synthesizing biologically important fluorine-containing compounds are limited,[12] the process provides a convenient new route to ketones containing fluoroalkyl groups or their derivatives.[13] The present process as well as the process utilizing carboxylic anhydrides[14] may serve as a general route to unsymmetrical ketones under mild conditions without using organic halides and a base.

Experimental

General Procedures. All manipulations were carried out under argon atmosphere using Schlenk tube techniques. Solvents were purified by the usual methods under argon. NMR spectra were recorded on a JEOL Lambda 500 spectrometer for ^1H (500 MHz, referenced to $SiMe_4$ via residual solvent protons), $^{13}C\{^1H\}$ (125 MHz, referenced to $SiMe_4$ via the solvent resonance), and ^{19}F (471 MHz, referenced to trifluoroacetic acid in $CDCl_3$ as an external standard) NMR. Coupling constants (J values) are given in hertz (Hz), and spin multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet), vt (virtual triplet), and br (broad). Gas chromatographic analyses (GC) were carried out on a GC-353 equipped with SE30. Low-resolution mass spectra were obtained with a JEOL JMS-Automass 150 that is coupled with gas chromatograph.

Reagents. All arylboronic acids were commercial products and were used without further purification. Phenyl trifluoroacetate purchased from Tokyo Kasei Kogyo Co. was distilled before use. All aryl perfluoroalkanecarboxylates except for phenyl trifluoroacetate were synthesized by the reaction of trifluoroacetic anhydride, pentafluoropropionic anhydride, and heptafluorobutyric anhydride with the corresponding phenols in the presence of sodium hydride. P^nBu_3 purchased from Kanto Kagaku Co. was distilled before use. All tertiary phosphines except for P^nBu_3 and $P(O^nBu)_3$ were commercial products and were used directly. *Trans*-$[PdEt_2(PMe_3)_2]$[15] and $Pd(dba)_2$[16] were synthesized by literature methods. $Pd(OAc)_2$ and 10% Pd/C were used as received from commercial suppliers.

***Trans*-[Pd(COCF$_3$)(OPh)(PMe$_3$)$_2$] 3** was prepared as previ-

ously reported[5] by the reaction of $[Pd(styrene)(PMe_3)_2]$[15] with phenyl trifluoroacetate.

Reaction of *trans*-[Pd(COCF$_3$)(OPh)(PMe$_3$)$_2$] 3 with Phenylboronic Acid 4 (Eq. 4). To an *N*-methyl-2-pyrrolidinone (NMP) solution (5 cm^3) of *trans*-[Pd(COCF$_3$)(OPh) (PMe$_3$)$_2$] (466 mg, 1.04 mmol), phenylboronic acid (127 mg, 1.04 mmol) was added at room temperature. The mixture was stirred for 1.5 h at room temperature. The GC and GC-MS analysis of the products was performed with $^nC_{14}H_{30}$ as an internal standard. Formation of phenyl trifluoromethyl ketone (66%) was confirmed. $CF_3COC_6H_5$ was characterized by GC-MS by comparing with an authentic sample (Aldrich). GC-MS *m/z* (rel. intensity) 174 (55), 105 (100), 95 (15).

Effect of Catalyst (Table 1). A typical procedure is as follows (Run 3). An NMP solution (5 cm^3) containing $Pd(OAc)_2$ (11.8 mg, 0.0525 mmol), tributylphosphine (0.038 cm^3, 15 mmol), phenyl trifluoroacetate (0.15 cm^3, 1.0 mmol), and phenylboronic acid (148 mg, 1.21 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C for 24 h.

Effect of Solvent and Temperature (Table 2). A typical procedure is as follows (Run 8). NMP solutions (5 cm^3) containing $Pd(OAc)_2$ (11.7 mg, 0.052 mmol), tributylphosphine (0.038 cm^3, 15 mmol), phenyl trifluoroacetate (0.15 cm^3, 1.0 mmol), and phenylboronic acid (149 mg, 1.22 mmol) in a 25 cm^3 Schlenk tube were heated under argon at room temperature, 60 °C, 80 °C, and 100 °C, respectively, for 24 h. The effects of solvents were examined in NMP, dioxane, toluene, acetonitrile, and DMF by carrying out the synthesis at 80 °C.

Synthesis of Trifluoromethyl Ketones (Table 3). A typical procedure is as follows (Run 4). An NMP solution (5 cm^3) containing $Pd(OAc)_2$ (11.5 mg, 0.051 mmol), tributylphosphine (0.038 cm^3, 0.15 mmol), phenyl trifluoroacetate (0.15 cm^3, 1.0 mmol), and 4-methoxyphenylboronic acid (185 mg, 1.22 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C for four hours. On cooling the reaction mixture, diethyl ether and H_2O were added and the aqueous layer was extracted with diethyl ether. The combined ether solution was dried ($MgSO_4$) and the solvent was evaporated in vacuo. Purification of the residue by column chromatography (hexane/Et_2O = 9:1) gave the corresponding product as a colorless oil (173 mg; yield 84%).

CF$_3$COC$_6$H$_4$-4-OMe:[13e] Colorless oil (84%); ^{1}H NMR (acetone-d_6, r. t., 500 MHz) δ 8.22–8.06 (m, 2H, aromatic H), 7.99–7.09 (m, 2H, aromatic H), 3.96 (s, 3H, OCH_3); $^{13}C\{^1H\}$ NMR (acetone-d_6, r. t., 125 MHz) δ 179.2 (q, $^2J_{CF}$ = 33.9 Hz, carbonyl C), 166.8 (s, aromatic C), 133.4 (q, $^3J_{CF}$ = 2.2 Hz, aromatic C), 123.3 (s, aromatic C), 117.9 (q, $^1J_{CF}$ = 291.2 Hz, *C*F$_3$), 115.7 (s, aromatic C), 56.4 (s, O*C*H$_3$); ^{19}F NMR (acetone-d_6, r. t., 471 MHz) δ –71.0 (s, C*F*$_3$). GC-MS *m/z* (rel intensity) 204 (83), 135 (92), 107 (100), 92 (98), 77 (97). Found: C, 53.18; H, 3.38%. Calcd for $C_9H_7F_3O_2$: C, 52.95; H, 3.46%.

The following trifluoromethyl ketones were synthesized by the above general procedure.

CF$_3$COC$_6$H$_5$:[13c,d,e] (81%); $CF_3COC_6H_5$ was characterized by GC-MS by comparison with an authentic sample (Aldrich). GC-MS *m/z* (rel intensity) 174 (60), 105 (100), 95 (20).

CF$_3$COC$_6$H$_4$-2-OMe: Yellow oil (68%); ^{1}H NMR (acetone-d_6, r. t., 500 MHz) δ 7.71–7.68 (m, 1H, aromatic H), 7.65–7.63 (m, 1H, aromatic H), 7.26–7.25 (m, 1H, aromatic H), 7.15–7.11 (m, 1H, aromatic H), 4.09 (s, 3H, OCH_3); $^{13}C\{^1H\}$ NMR (acetone-d_6, r. t., 125 MHz) δ 184.3 (q, $^2J_{CF}$ = 36.3 Hz, carbonyl C), 160.5 (s, aromatic C), 136.9 (s, aromatic C), 131.7 (s, aromatic C), 122.8 (s, aromatic C), 121.7 (s, aromatic C), 117.1 (q, $^1J_{CF}$ = 290.6 Hz, *C*F$_3$), 113.4 (s, aromatic C), 56.5 (s, O*C*H$_3$); ^{19}F NMR (acetone-d_6, r. t., 471 MHz) δ –73.4 (s, C*F*$_3$). GC-MS *m/z* (rel intensity) 204 (100), 135 (97), 105 (37), 92 (98). Found: C, 52.58; H, 3.20%. Calcd for $C_9H_7F_3O_2$: C, 52.95; H, 3.46%.

CF$_3$COC$_6$H$_4$-3-OMe: Colorless oil (78%); ^{1}H NMR (acetone-d_6, r. t., 500 MHz) δ 7.67–7.65 (m, 1H, aromatic H), 7.60–7.57 (m, 1H, aromatic H), 7.54 (br, 1H, aromatic H), 7.41–7.39 (m, 1H, aromatic H), 3.90 (s, 3H, OCH_3); $^{13}C\{^1H\}$ NMR (acetone-d_6, r. t., 125 MHz) δ 180.8 (q, $^2J_{CF}$ = 34.6 Hz, carbonyl C), 161.2 (s, aromatic C), 131.9 (s, aromatic C), 123.1 (q, $^3J_{CF}$ = 2.6 Hz aromatic C), 117.6 (q, $^1J_{CF}$ = 291.0 Hz, *C*F$_3$), 114.9 (q, $^4J_{CF}$ = 1.9 Hz, aromatic C), 56.0 (q, $^7J_{CF}$ = 2.8 Hz, O*C*H$_3$); ^{19}F NMR (acetone-d_6, r. t., 471 MHz) δ –70.0 (s, C*F*$_3$). GC-MS *m/z* (rel. intensity) 204 (100), 135 (97), 107 (86), 92 (92), 77 (99). Found: C, 52.86; H, 3.20%. Calcd for $C_9H_7F_3O_2$: C, 52.95; H, 3.46%.

CF$_3$COC$_6$H$_4$-4-Me:[13e] Colorless oil (74%); ^{1}H NMR (acetone-d_6, r. t., 500 MHz) δ 7.98 (d, 2H, $^3J_{HH}$ = 8.22 Hz aromatic H), 7.48 (d, 2H, $^3J_{HH}$ = 8.22 Hz aromatic H), 2.46 (s, 3H, CH_3); $^{13}C\{^1H\}$ NMR (acetone-d_6, r. t., 125 MHz) δ 180.5 (q, $^2J_{CF}$ = 34.4 Hz, carbonyl C), 148.4 (s, aromatic C), 130.9 (s, aromatic C), 130.9 (q, $^3J_{CF}$ = 2.2 Hz, aromatic C), 128.2 (s, aromatic C), 117.8 (q, $^1J_{CF}$ = 291.2 Hz, *C*F$_3$), 21.8 (s, *C*H$_3$); ^{19}F NMR (acetone-d_6, r. t., 471 MHz) δ –70.0 (s, C*F*$_3$). GC-MS *m/z* (rel intensity) 188 (61), 119 (96), 91 (98).

CF$_3$COC$_6$H$_4$-3-CF$_3$: (66%); $CF_3COC_6H_4$-3-CF_3 was characterized by GC-MS on comparison with an authentic sample (Aldrich). GC-MS *m/z* (rel intensity) 223 (14), 173 (100), 145 (98), 125 (13), 95 (20).

CF$_3$COC$_6$H$_4$-4-CF$_3$: (17%); $CF_3COC_6H_4$-4-CF_3 was characterized by GC-MS on comparison with an authentic sample (Aldrich). GC-MS *m/z* (rel intensity) 223 (10), 173 (100), 145 (92), 125 (12), 95 (15).

CF$_3$CO-1-C$_{10}$H$_7$:[13b,e] Colorless oil (66%); ^{1}H NMR (acetone-d_6, r. t., 500 MHz) δ 8.75–8.74 (m, 1H, aromatic H), 8.35–8.33 (m, 1H, aromatic H), 8.29–8.27 (m, 1H, aromatic H), 8.08–8.07 (m, 1H, aromatic H), 7.76–7.71 (m, 2H, aromatic H), 7.69–7.66 (m, 1H, aromatic H); $^{13}C\{^1H\}$ NMR (acetone-d_6, r. t., 125 MHz) δ 182.3 (q, $^2J_{CF}$ = 33.3 Hz, carbonyl C), 137.2 (s, aromatic C), 135.0 (s, aromatic C), 132.5 (q, $^3J_{CF}$ = 3.8 Hz, aromatic C), 131.8 (s, aromatic C), 130.3 (s, aromatic C), 130.1 (s, aromatic C), 128.1 (s, aromatic C), 127.2 (s, aromatic C), 125.7 (s, aromatic C), 125.4 (s, aromatic C), 117.6 (q, $^1J_{CF}$ = 292.9 Hz, *C*F$_3$); ^{19}F NMR (acetone-d_6, r. t., 471 MHz) δ –69.1 (s, C*F*$_3$). GC-MS: *m/z* (rel intensity) 224 (73), 155 (100), 127 (91).

CF$_3$CO-2-C$_{10}$H$_7$:[13e] Yellow powder (72%); ^{1}H NMR (acetone-d_6, r. t., 500 MHz) δ 8.75 (s, 1H, aromatic H), 8.25–8.23 (m, 1H, aromatic H), 8.14–8.12 (m, 1H, aromatic H), 8.06–8.05 (m, 2H, aromatic H), 7.79–7.76 (m, 1H, aromatic H), 7.71–7.68 (m, 1H, aromatic H); $^{13}C\{^1H\}$ NMR (acetone-d_6, r. t., 125 MHz) δ 180.9 (q, $^2J_{CF}$ = 34.4 Hz, carbonyl C), 137.4 (s, aromatic C), 133.9 (q, $^3J_{CF}$ = 2.8 Hz, aromatic C), 133.2 (s, aromatic C), 131.2 (s, aromatic C), 131.1 (s, aromatic C), 130.2 (s, aromatic C), 128.8 (s, aromatic C), 128.5 (s, aromatic C), 128.0 (s, aromatic C), 124.7 (q, $^4J_{CF}$ = 1.6 Hz, aromatic C), 117.8 (q, $^1J_{CF}$ = 291.2 Hz, *C*F$_3$); ^{19}F NMR (acetone-d_6, r. t., 471 MHz) δ –70.3 (s, C*F*$_3$). GC-MS *m/z* (rel intensity) 224 (100), 155 (95), 127 (94).

Synthesis of Other Perfluoroalkyl Ketones (Eq. 5). Applicability of the process for other phenyl perfluoroalkanecarboxylates was examined. A typical procedure using phenyl heptafluorobutyrate is given below. An NMP solution (5 cm^3) containing $Pd(OAc)_2$ (11.7 mg, 0.052 mmol), tributylphosphine (0.038 cm^3,

0.15 mmol), heptafluorobutyrate (295 mg, 1.02 mmol), and 4-methoxyphenylboronic acid (181 mg, 1.19 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C for four hours. After the reaction mixture was cooled, diethyl ether and H_2O were added and the aqueous layer was extracted with diethyl ether. The combined ether solution was dried ($MgSO_4$) and the solvent was evaporated in vacuo. Purification of the residue by column chromatography (hexane/Et_2O = 13:1) gave the corresponding product as a colorless oil (271 mg; yield 87%).

$C_3F_7COC_6H_4$-4-OMe: Colorless oil (87%); ^{1}H NMR (acetone-d_6, r. t., 500 MHz) δ 8.09 (m, 2H, aromatic H), 7.18–7.11 (m, 2H, aromatic H), 3.96 (s, 3H, OCH_3); ^{13}C{^{1}H} NMR (acetone-d_6, r. t., 125 MHz) δ 181.8 (t, $^2J_{CF}$ = 25.2 Hz, carbonyl C), 166.9 (s, aromatic C), 133.7 (q, $^3J_{CF}$ = 3.6 Hz, aromatic C), 124.9 (s, aromatic C), 118.7 (qt, $^1J_{CF}$ = 287.0 Hz, $^2J_{CF}$ = 34.0 Hz, CF_3), 115.7 (s, aromatic C), 111.7 (tt, $^1J_{CF}$ = 268.0 Hz, $^2J_{CF}$ = 31.5 Hz, COCF_2CF_2), 112.3–107.2 (m, $CF_2CF_2CF_3$), 56.4 (s, OCH_3); ^{19}F NMR (acetone-d_6, r. t., 471 MHz) δ –79.0 (t, $^3J_{FF}$ = 9.2 Hz, $CF_2CF_2CF_3$), –111.7 (q, $^3J_{FF}$ = 9.2 Hz, $CF_2CF_2CF_3$), –124.2 (s, COCF_2CF_2). GC-MS *m/z* (rel intensity) 304 (100), 285 (32), 257 (31), 207 (7), 169 (22), 135 (93), 107 (98), 92 (97), 76 (99). Found: C, 43.54; H, 2.02%. Calcd for $C_{11}H_7F_7O_2$: C, 43.44; H, 2.32%.

$C_2F_5COC_6H_4$-4-OMe: Colorless oil (86%); ^{1}H NMR (acetone-d_6, r. t., 500 MHz) δ 8.09 (m, 2H, aromatic H), 7.15 (m, 2H, aromatic H), 3.96 (s, 3H, OCH_3); ^{13}C{^{1}H} NMR (acetone-d_6, r. t., 125 MHz) δ 181.9 (t, $^2J_{CF}$ = 26.0 Hz, carbonyl C), 166.9 (s, aromatic C), 133.5 (q, $^3J_{CF}$ = 3.4 Hz, aromatic C), 124.4 (s, aromatic C), 118.7 (qt, $^1J_{CF}$ = 286.0 Hz, $^2J_{CF}$ = 35.4 Hz, CF_3), 115.7 (s, aromatic C), 111.7 (tq, $^1J_{CF}$ = 268.6 Hz, $^2J_{CF}$ = 35.4 Hz, COCF_2CF_3), 56.4 (s, OCH_3); ^{19}F NMR (acetone-d_6, r. t., 471 MHz) δ –80.5 (s, CF_3), –113.7 (s, CF_2CF_3). GC-MS *m/z* (rel intensity) 254 (53), 207 (17), 157 (14), 135 (97), 107 (83), 92 (100), 76 (91). Found: C, 47.40; H, 2.51%. Calcd for $C_{10}H_7F_5O_2$: C, 47.26; H, 2.78%.

Cross-Coupling Reaction of Phenyl Trifluoroacetate with Other Organoboron Compounds (Eq. 6). A typical procedure using $NaBPh_4$ is given below. An NMP solution (5 cm^3) containing $Pd(OAc)_2$ (11.8 mg, 0.0525 mmol), tributylphosphine (0.038 cm^3, 15 mmol), phenyl trifluoroacetate (0.15 cm^3, 1.0 mmol), and sodium tetraphenylborate (416 mg, 1.22 mmol) in a 25 cm^3 Schlenk tube was heated under argon at 80 °C for four hours. The yields of phenyl trifluoromethyl ketone were determined by GC using $^nC_{14}H_{30}$ as an internal standard.

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References

1 a) J. Tsuji, "Palladium Reagents and Catalysts, Innovations in Organic Synthesis," Wiley, Chichester (1995); b) J. P. Collman, L. S. Hegedus, J. N. Norton, and R. G. Finke, "Principles and Applications of Organotransition Metal Chemistry," University Science Books, California (1987); c) A. Yamamoto, "Organotransition Metal Chemistry," Wiley-Interscience, New York (1986).

2 a) A. Yamamoto, *Adv. Organometal. Chem.*, **34**, 111 (1992); b) Y. -S. Lin and A. Yamamoto, "Topics in Organometallic Chemistry," ed by S. Murai, Springer, Berlin (1999), Vol. 3, pp. 161–192.

3 a) J. Ishizu, T. Yamamoto, and A. Yamamoto, *Chem. Lett.*, **1976**, 1091; b) T. Yamamoto, J. Ishizu, T. Kohara, S. Komiya, and A. Yamamoto, *J. Am. Chem. Soc.*, **102**, 3758 (1980); c) T. Yamamoto, J. Ishizu, and A. Yamamoto, *J. Am. Chem. Soc.*, **103**, 6863 (1981); d) T. Yamamoto, J. Ishizu, and A. Yamamoto, *Bull. Chem. Soc. Jpn.*, **55**, 623 (1982); e) T. Yamamoto, M. Akimoto, O. Saito, and A. Yamamoto, *Organometallics*, **5**, 1559 (1986); f) S. Komiya, A. Yamamoto, and T. Yamamoto, *Chem. Lett.*, **1981**, 193; g) K. Sano, T. Yamamoto, and A. Yamamoto, *Chem. Lett.*, **1983**, 115; h) K. Sano, T. Yamamoto, and A. Yamamoto, *Bull. Chem. Soc. Jpn.*, **57**, 2741 (1984).

4 a) K. Nagayama, F. Kawataka, M. Sakamoto, I. Shimizu, and A. Yamamoto, *Chem. Lett.*, **1995**, 367; b) K. Nagayama, F. Kawataka, M. Sakamoto, I. Shimizu, and A. Yamamoto, *Bull. Chem. Soc. Jpn.*, **72**, 573 (1999).

5 K. Nagayama, I. Shimizu, and A. Yamamoto, *Bull. Chem. Soc. Jpn.*, **72**, 799 (1999).

6 K. Nagayama, I. Shimizu, and A. Yamamoto, *Chem. Lett.*, **1998**, 1143.

7 For a recent review on palladium-catalyzed cross-coupling reaction of organoboron compounds. a) N. Miyaura and A. Suzuki, *Chem. Rev.*, **95**, 2457 (1995); b) A. Suzuki, *J. Organomet. Chem.*, **576**, 147 (1999).

8 Palladium catalyzed cross-coupling reactions to give ketones with acyl halides and organoboron compounds such as phenylboronic acids and sodium arylborates have been reported. a) C. S. Cho, K. Itotani, and S. Uemura, *J. Organomet. Chem.*, **443**, 253 (1993); b) N. A. Bumagin and D. N. Korolev., *Tetrahedron Lett.*, **40**, 3057 (1999); c) M. Haddach and J. R. McCarthy, *Tetrahedron Lett.*, **40**, 3109 (1999); d) G. W. Kabalka, R. R. Malladi, D. Tejedor, and S. Kelley, *Tetrahedron Lett.*, **41**, 999 (2000). e) H. Chen and M.-Z. Deng, *Org. Lett.*, **2**, 1649 (2000).

9 a) F. Ozawa, A. Kubo, and T. Hayashi, *Chem. Lett.*, **1992**, 2177; b) C. Amatore, A. Jutand, and M. A. M'Barki, *Organometallics*, **11**, 3009 (1992); c) T. Mandai, T. Matsumoto, J. Tsuji, and S. Saito, *Tetrahedron Lett.*, **34**, 2513 (1993).

10 Cross-coupling reaction of sterically hindered arylboronic acids with organic electrophiles is known to proceed ineffectively. W. J. Thompson and J. Gaudino, *J. Org. Chem.*, **49**, 5237 (1984).

11 a) T. Ishiyama, M. Murata, and N. Miyaura, *J. Org. Chem.*, **60**, 7508 (1995); b) N. Miyaura, K. Yamada, H. Suginome, and A. Suzuki, *J. Am. Chem. Soc.*, **107**, 972 (1985). Reports on palladium-catalyzed cross-coupling reaction of organic compounds with organoboron reagents under neutral conditions. c) T. Moriya, N. Miyaura, and A. Suzuki, *Synlett*, **1994**, 149; d) F. Sasaya, N. Miyaura, and A. Suzuki, *Bull. Korean Chem. Soc.*, **8**, 329 (1987).

12 a) J. K. Liebman, A. Greenberg, and W. R. Dolbier, Jr., "Fluorine-containing Molecules, Structure, Reactivity, Synthesis," VCH, New York (1998); b) "Synthetic Fluorine Chemistry," ed by G. A. Olah, R. D. Chambers, and G. K. S. Prakash, John Wiley & Sons, New York (1992); c) "Selective Fluorination in Organic and Bioorganic Chemistry," ed by J. T. Welsh, ACS Symposium Series 456 (1990).

13 The general methods for synthesizing of trifluoromethyl ketones. a) J. -P. Bague, D. Bonnet-Delphon, *Tetrahedron*, **47**, 3207 (1991); b) Y. Yokoyama and K. Mochida, *Synlett*, **1997**, 907; c) J. Wiedemann, T. Heiner, G. Mloston, G. K. S. Prakash, and G. A. Olah, *Angew. Chem., Int. Ed. Engl.*, **37**, 820 (1998); d) R. P. Singh, G. Cao, R. L. Kirchmeier, and J. M. Shreeve, *J. Org. Chem.*, **64**, 2873 (1999). e) T. Keumi, M. Shimada, M. Takahashi, and H. Kitajima, *Chem. Lett.*, **1990**, 783.

14 Results to be reported separately.

15 Y.-J. Kim, K. Osakada, A. Takenaka, and A. Yamamoto, *J. Am. Chem. Soc.*, **112**, 1096 (1990).

16 T. Ukai, H. Kawazura, Y. Ishii, J. J. Bonnet, and J. A. Ibers, *J. Organomet. Chem.*, **65**, 253 (1974).