Formation of Quaternary Carbon Center with a Trifluoromethyl Group Using a Pd-Catalyzed Allylation Reaction

Kazuyuki SATO, Yu TAKIGUCHI, Yosuke YOSHIZAWA, Kayoko IWASE, Yoshie SHIMIZU, Atsushi TARUI, Masaaki OMOTE, Itsumaro KUMADAKI, and Akira ANDO*

Faculty of Pharmaceutical Sciences, Setsunan University; 45–1 Nagaotoge-cho, Hirakata, Osaka 573–0101, Japan.
Received June 12, 2007; accepted August 21, 2007; published online August 22, 2007

Synthesis of compounds with quaternary carbons is one of the most attractive reactions in the synthetic chemistry. However, there are only a few reports on synthesis of the compounds with a fluoroalkyl group at a quaternary carbon center. Recently, we reported the synthesis of α-trifluoromethylated ketones by the reaction of α,β-unsaturated ketones with CF_3-I using a Rh catalyst. When the α-trifluoromethylated ketones and allyl carbonates were treated with a Pd catalyst, the allylation reaction proceeded smoothly at the trifluoromethylated carbon to give the desired compounds with a trifluoromethylated quaternary carbon center in good to excellent yields.

Key words fluorine; quaternary carbon; palladium catalyst; allylation reaction

Organofluorine compounds have significantly interesting features, which are used in the field of bioactive materials as medicine or agricultural chemicals and functional materials as polymers or liquid crystals.[1—3] Therefore, many people have actively investigated the synthesis and/or the reaction of fluorinated compounds, and there are a lot of reports about them.[4—6]

On the other hand, the formation of a quaternary carbon center has recently attracted great attention in synthetic organic chemistry.[7—10] For example, the bioactive compounds such as carotenoids or steroids contain one or more quaternary carbon center(s) in their molecules, and their synthesis is an important subject of research. However, there are only a few reports on the formation of a quaternary carbon–carbon bond with a fluorinated substituent.[11—15]

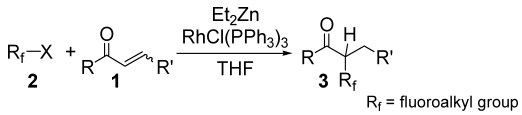


Chart 1

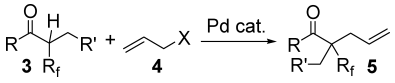


Chart 2

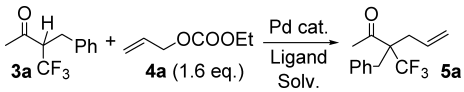
Recently, we have reported the synthesis of α-trifluoromethylated ketones[16,17] or α-fluoroalkylated ketones[18] from α,β-unsaturated ketones (**1**) by the reaction of trifluoromethyl iodide or α,α-difluoro halogen compounds (**2**) in the presence of Et_2Zn and $RhCl(PPh_3)_3$ (Chart 1).

Herein, we would like to report the Pd-catalyzed allylation reaction of **3** for the formation of a quaternary carbon center that has a fluoroalkyl group (Chart 2).

Discussion

The compounds (**3**) have a highly acidic hydrogen on the methine carbon that has the carbonyl group and the fluoro-

Table 1. Examination of Reaction Conditions

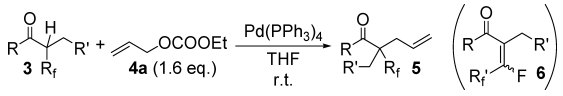


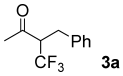
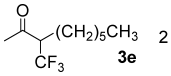
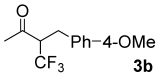
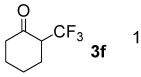
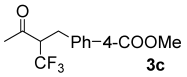
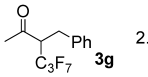
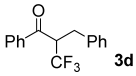
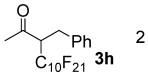
Entry	Pd catalyst	Amount of Pd (mol%)	Ligand (eq)	Solv.	Time (h)	Yield[a] of **5a** (%)
1	$Pd(PPh_3)_4$	4	None	Et_2O	3	91
2	$Pd(PPh_3)_4$	4	None	THF	1.5	Quant. (96)[b]
3	$Pd(PPh_3)_4$	4	None	CH_2Cl_2	25	73
4	$Pd(PPh_3)_4$	4	None	Hexane	6	66
5	$Pd(PPh_3)_4$	4	None	DMF	1	60
6	$Pd(PPh_3)_4$	4	None	CH_3CN	9	73
7	None	—	None	THF	3	nr[c]
8	$Pd(PPh_3)_4$	2	None	THF	6	69
9	$Pd(PPh_3)_4$	10	None	THF	1.5	92
10	None	—	PPh_3 (0.1)	THF	24	nr[c]
11	$PdCl_2$	4	None	THF	24	nr[c]
12	$PdCl_2$	4	PPh_3 (0.1)	THF	24	nr[c]
13	$Pd(OAc)_2$	4	None	THF	10	nr[c]
14	$Pd(OAc)_2$	4	PPh_3 (0.1)	THF	2	89

a) ^{19}F-NMR yield. *b*) Isolated yield. *c*) Recovered the starting material (**3a**).

* To whom correspondence should be addressed. e-mail: aando@pharm.setsunan.ac.jp

Table 2. Allylation of Various **3**



Entry	3	Time (h)	Yield (%)[a]	Entry	3	Time (h)	Yield (%)[a]
1	 **3a**	1.5	96	5	 **3e**	2	2	54
2	 **3b**	1	92	6	 **3f**	1	1	73
3	 **3c**	1	93	7	 **3g**	2.5	2.5	0 (58)[b]
4	 **3d**	0.5	61	8	 **3h**	2	2	0 (38)[b]

a) Isolated yield. *b*) The yield of **6** was shown in parenthesis.

alkyl group (R_f) on both sides. At first, we examined the reaction of **3** with aldehydes under a basic condition. Unfortunately, we could not create a quaternary carbon center on the methine carbon at all, since dehydrofluorination proceeded in basic condition.

Now, we attempted the Pd-catalyzed allylation reaction of **3** to generate a quaternary carbon as an expansion of applicability of our α-fluoroalkylation reaction (Chart 2). Our idea is: If this reaction would proceed successfully, a chiral fluoroalkylated quaternary carbon center could be formed, since it is well-known that Pd-catalyzed allylation reactions proceed under a neutral condition, and have the ability for synthesizing the asymmetric product.

About half a decade ago, Kitazume and his co-workers reported a Pd-catalyzed allylation of ethyl 3,3,3-trifluoropropionate.[19,20] Furthermore, recently, Ishihara and his co-workers reported a Pd-catalyzed allylation of trifluoroalanine derivatives.[21] They obtained the products which was forming a carbon-carbon bond at the active methylene carbon in moderate to good yields. So, we applied their condition to our compound (**3**) to construct a quaternary carbon center.

At first, 3-benzyl-4,4,4-trifluorobutan-2-one (**3a**) was chosen as the substrate, and it was treated with allyl ethyl carbonate (**4a**) in the presence of 4 mol% of $Pd(PPh_3)_4$ in Et_2O. As expected, the desired product (**5a**) was obtained in an excellent yield even when the reaction was carried out at room temperature. Based on the examination of various reaction conditions shown in Table 1, we found that entry 2 gave the best result.

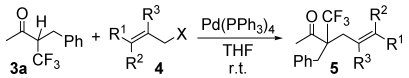
As shown in entries 7 and 10, the product was not obtained at all when a Pd catalyst was not added or only PPh_3 was added without palladium. Furthermore, the yield was not affected by increasing the amount of a Pd catalyst (entry 9). The product was obtained in a good yield when $Pd(OAc)_2$ was used as a Pd salt with PPh_3 (entry 14). This suggests that the reaction could be extended to an asymmetric reaction using chiral phosphine as a ligand.

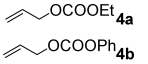
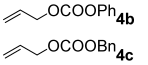
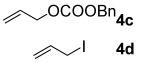
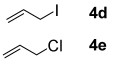
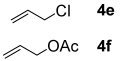
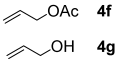
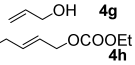
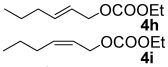
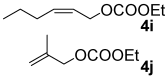
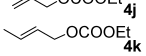
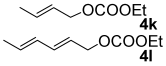
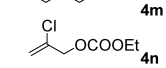
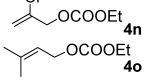
Next, we examined the allylation reaction of various fluoroalkyl ketones **3**. The results are summarized in Table 2.

As shown in entries 1—3, the substituents on the phenyl group did not have significant effects on the yields of the products, and the desired products (**5**) were obtained in excellent yields. α-Trifluoromethyl ketone with an aryl group on the carbonyl group or fully aliphatic ones also reacted smoothly to give the products in moderate to good yields (entries 4—6). However, the ketones (**3g**, **h**) that have a longer fluoroalkyl chain did not afford the desired products (**5g**, **h**) at all as shown in entries 7 and 8, and gave the dehydrofluorinated compounds (**6g**, **h**) in moderate yields probably because their steric effects hindered the introduction of the allyl group.

Finally, we examined the reaction using various allyl compounds (**4**). The results are shown in Table 3.

Table 3. Examination of Effects of Substituents of **4** on the Reaction



Entry	4	Time (h)	5	
			Product	Yield (%)[a]
1	 **4a**	1.5	**5a**	96
2	 **4b**	0.5	**5a**	23
3	 **4c**	1.5	**5a**	89
4	 **4d**	24	**5a**	nr[b]
5	 **4e**	24	**5a**	nr[b]
6	 **4f**	10	**5a**	nr[b]
7	 **4g**	24	**5a**	nr[b]
8	 **4h**	4.5	**5i**	87[c]
9	 **4i**	2.5	**5i**	92[c]
10	 **4j**	1.5	**5j**	91
11	 **4k**	1.5	**5k**	72[d]
12	**4l**	2	**5l**	68[e]
13	 **4m**	2.5	**5m**	90[c]
14	 **4n**	3	**5n**	nr[b]
15	**4o**	1.5	**5o**	nd[f]

a) Isolated yield. *b*) Compound **4** was recovered. *c*) Only *E* product. *d*) *E*/*z* mixture (5 : 1). *e*) *E*/*z* mixture (7 : 1). *f*) Compound **4** was decomposed.

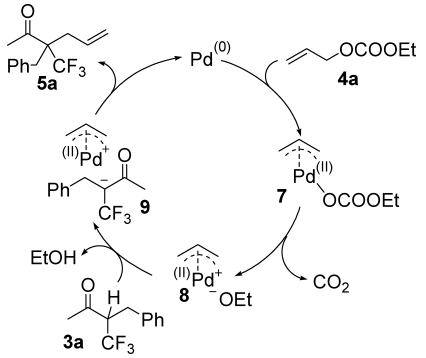


Fig. 1. Tentative Reaction Mechanism

The leaving group of **4** played an important role. Thus, carbonates gave the products in good to excellent yields except the allyl phenyl carbonate (**4b**) (entries 1—3). It might be attributed to the fact that the basicity of the phenoxide derived from **4b** with a Pd catalyst is weaker than the ethoxide or the benzyloxide. The weakness of a basicity or the steric hindrance would lead to the decrease of the yield.

Next, we examined the effect of the substituents on the double bond (entries 8—15 in Table 3). All products were obtained in satisfactory yields except in entries 14 and 15. In entries 8 and 9, the same product (**5i**; *E*-form) was obtained from both isomers (**4h**, **i**). This means that the intermediate might be the same π-allyl palladium complex. Furthermore, when the reactions proceeded smoothly, the substitution occurred at a less hindered position. On the other hand, **4n** was recovered from the reaction mixture, while **4o** was decomposed (entries 14, 15).

The above Pd-catalyzed allylation reaction is explained the mechanism shown in Fig. 1.[22] The π-allyl alkoxy palladium complex (**8**), that derived from the oxidative addition of the Pd catalyst into **4** followed by the decarboxylation, reacts with **3**, resulting in the formation of **9** after deprotonation of **3**. In the next step, the reductive elimination afforded the product (**5**) and regenerated the Pd(0) catalyst. In this reaction mechanism, **4n** might not afford the complex **7** because the oxidative addition with a Pd catalyst was inhibited by the low electron density caused by the chlorine. On the other hand, **4o** could not afford the complex **9** owing to the steric hindrance, even if the complex (**8**) might be formed.

Conclusion

We obtained allyl compounds (**5**) with a trifluoromethyl group at a quaternary carbon center in good to excellent yields at room temperature. Only allyl carbonates (**4**) could be used as allyl component for this reaction, and the substitution occurred regioselectively at the less hindered position of the allyl groups. Now, we are trying to apply this reaction for the formation of an asymmetric quaternary carbon center.

Experimental

General Informations ^{1}H- and ^{13}C-NMR spectra were recorded on JNM-GX400 spectrometers. Tetramethylsilane (TMS) was used as an internal standard. ^{19}F-NMR spectra were recorded on Hitachi FT-NMR R-1500 and JEOL-ECA-600SN spectrometers. Benzotrifluoride (BTF) was used as an internal standard. Mass spectra were obtained on JEOL JMS-700T spectrometers. IR spectra were recorded on Hitachi 270-30 Infrared spectrophotometer. Gas-liquid chromatography (GLC) was carried out on a Hitachi 263-50 gas chromatograph (column; 5% SE-30 3 mm×2 m, carrier; N_2 at 30 ml/min). Peak areas were calculated on a Shimadzu C-R5A Chromatopac. Melting points were measured on Yanagimoto micro melting point apparatus MP-S3. All the solvents were purified by standard procedure under an Ar atmosphere, and other commercially available reagents were used without further purification.

Typical Procedures Under an Ar atmosphere, to a solution of $Pd(PPh_3)_4$ (23.1 mg, 0.02 mmol) in THF (4 ml) was added 3-benzyl-4,4,4-trifluorobutan-2-one (**3a**, 108.1 mg, 0.5 mmol) and allyl ethyl carbonate (**4a**, 105.0 mg, 0.8 mmol), then the mixture was stirred for 1.5 h at room temperature. The solution was quenched with 10% HCl, and extracted with Et_2O. The Et_2O layer was washed with sat. NaCl and dried over $MgSO_4$. The solvent was removed *in vacuo* and purified by column chromatography (SiO_2, AcOEt : hexane = 1 : 9) to give 3-benzyl-3-(trifluoromethyl)-hex-5-en-2-one (**5a**, 123.1 mg, 96%).

Spectral Data 3-Benzyl-3-(trifluoromethyl)hex-5-en-2-one (**5a**): Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 2.27 (3H, q, J=2.0 Hz), 2.46 (1H, dd, J=14.4, 7.8 Hz), 2.64 (1H, dd, J=14.4, 6.5 Hz), 3.07 (1H, d, J=14.3 Hz), 3.18 (1H, d, J=14.3 Hz), 5.05 (1H, m), 5.13 (1H, m), 5.71 (1H, m), 7.10—7.14 (2H, m), 7.21—7.29 (3H, m). ^{13}C-NMR ($CDCl_3$) δ: 202.8, 134.6, 131.8, 130.5, 128.2, 127.1, 126.6 (q, J=284.3 Hz), 119.3, 61.9 (q, J=22.0 Hz), 37.9—38.0 (m), 36.4—36.5 (m), 28.6—28.8 (m). ^{19}F-NMR ($CDCl_3$) δ: −2.09 (3F, s). IR (neat) cm^{-1}: 3096, 3044, 2988, 2940, 1724, 1166. MS *m/z*: 256 (M^+); HR-MS Calcd for $C_{14}H_{15}F_3O$: 256.108 (M^+), Found: 256.108 (M^+).

3-(4-Methoxybenzyl)-3-(trifluoromethyl)hex-5-en-2-one (**5b**): Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 2.25 (3H, q, J=1.0 Hz), 2.43 (1H, dd, J=14.8, 7.8 Hz), 2.62 (1H, dd, J=14.8, 6.5 Hz), 3.01 (1H, d, J=14.5 Hz), 3.10 (1H, d, J=14.5 Hz), 3.75 (3H, d, J=1.6 Hz), 5.09 (1H, m), 5.12 (1H, m), 5.70 (1H, m), 6.79 (2H, m), 7.03 (2H, m). ^{13}C-NMR ($CDCl_3$) δ: 203.9, 159.3, 132.5, 126.7 (q, J=284.7 Hz), 126.4, 119.1, 113.6, 62.0 (q, J=21.7 Hz), 55.0—55.1 (m), 37.2 (q, J=1.7 Hz), 36.4—36.5 (m), 28.7—28.8 (m). ^{19}F-NMR ($CDCl_3$) δ: −2.09 (3F, s). IR (neat) cm^{-1}: 3092, 3008, 2940, 1720, 1186. MS *m/z*: 286 (M^+); HR-MS Calcd for $C_{15}H_{17}F_3O_2$: 286.118 (M^+), Found: 286.117 (M^+).

Methyl 4-[2-Acetyl-2-(trifluoromethyl)pent-4-enyl]benzoate (**5c**): Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 2.28 (3H, q, J=1.1 Hz), 2.49 (1H, dd, J=14.5, 7.8 Hz), 2.62 (1H, dd, J=14.5, 6.8 Hz), 3.05 (1H, d, J=14.0 Hz), 3.28 (1H, d, J=14.0 Hz), 3.90 (3H, s), 5.11—5.17 (2H, m), 5.68 (1H, m), 7.24 (2H, m), 8.00 (2H, m). ^{13}C-NMR ($CDCl_3$) δ: 202.5, 166.7, 140.4, 131.2, 130.6, 129.3, 129.0, 126.5 (q, J=284.4 Hz), 119.8, 62.0 (q, J=22.2 Hz), 52.1, 37.5—37.6 (m), 36.7—36.8 (m), 28.6—28.8 (m). ^{19}F-NMR ($CDCl_3$) δ: −1.94 (3F, s). IR (neat) cm^{-1}: 3432, 3092, 2956, 1728, 1186. MS *m/z*: 314 (M^+); HR-MS Calcd for $C_{16}H_{17}F_3O_3$: 314.113 (M^+), Found: 314.113 (M^+).

2-Benzyl-2-trifluoromethyl-1-phenylpent-4-en-1-one (**5d**): Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 2.66 (1H, dd, J=15.3, 7.5 Hz), 2.87 (1H, dd, J=15.3, 6.6 Hz), 3.36 (1H, d, J=14.2 Hz), 3.45 (1H, d, J=14.2 Hz), 5.05 (1H, m), 5.07 (1H, m), 5.70 (1H, m), 7.15—7.49 (10H, m). ^{13}C-NMR ($CDCl_3$) δ: 200.3, 139.7, 134.6, 131.7, 131.0, 130.7, 128.2, 127.2, 126.9, 126.3 (q, J=284.5 Hz), 119.4, 62.3 (q, J=21.1 Hz), 38.4—38.5 (m), 36.8—37.0 (m). ^{19}F-NMR ($CDCl_3$) δ: −1.55 (3F, s). IR (neat) cm^{-1}: 3072, 3040, 2988, 2940, 1690, 1180. MS *m/z*: 318 (M^+); HR-MS Calcd for $C_{19}H_{17}F_3O$: 318.123 (M^+), Found: 318.123 (M^+).

3-Allyl-3-(trifluoromethyl)nonan-2-one (**5e**): Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.7 Hz), 1.18—1.32 (8H, m), 1.70—1.87 (2H, m), 2.27 (3H, s), 2.50 (1H, dd, J=14.8, 7.3 Hz), 2.60 (1H, dd, J=14.8, 6.8 Hz), 5.11 (1H, m), 5.14 (1H, m), 5.70 (1H, m). ^{13}C-NMR ($CDCl_3$) δ: 203.1, 132.0, 126.8 (q, J=284.5 Hz), 119.1, 60.4 (q, J=22.1 Hz), 35.5—35.6 (m), 31.5, 31.3—31.4 (m), 29.8, 27.6—27.8 (m), 23.7, 22.6, 14.0. ^{19}F-NMR ($CDCl_3$) δ: −3.61 (3F, s). IR (neat) cm^{-1}: 3092, 2928, 2864, 1726, 1178. MS *m/z*: 250 (M^+); HR-MS Calcd for $C_{13}H_{21}F_3O$: 250.154 (M^+), Found: 250.155 (M^+).

2-Allyl-2-(trifluoromethyl)cyclohexanone (**5f**): Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.75—2.07 (6H, m), 2.43—2.52 (3H, m), 2.67 (1H, dd, J=14.6, 6.6 Hz), 5.11—5.18 (2H, m), 5.64—5.76 (1H, m). ^{13}C-NMR ($CDCl_3$) δ: 205.3, 131.8, 126.4 (q, J=284.8 Hz), 119.6, 56.9 (q, J=21.9 Hz), 40.3—40.4 (m), 35.7—35.8 (m), 30.4—30.5 (m), 25.7, 20.4. ^{19}F-NMR ($CDCl_3$) δ: −7.28 (3F, s). IR (neat) cm^{-1}: 2956, 2880, 1724, 1226. MS *m/z*: 206 (M^+); HR-MS Calcd for $C_{10}H_{13}F_3O$: 206.092 (M^+), Found: 206.092 (M^+).

3-Benzyl-4,5,5,6,6,6-hexafluorohex-3-en-2-one (**6g**): Yellow oil. ^{1}H-NMR ($CDCl_3$) δ: 2.25 (3H, d, J=4.4 Hz), 3.79 (2H, d, J=1.5 Hz), 7.12—7.16 (2H, m), 7.22—7.33 (3H, m). ^{19}F-NMR ($CDCl_3$) δ: −56.3 (1F, bs), −53.1—−53.2 (2F, m), −21.0—−21.2 (3F, m). IR (neat) cm^{-1}: 3072, 3040, 1716, 1228. MS *m/z*: 296 (M^+); HR-MS Calcd for $C_{13}H_{10}F_6O$: 296.064 (M^+), Found: 296.064 (M^+).

3-Benzyl-4-fluoro-4-perfluorononylbut-3-en-2-one (**6h**): Colorless crys-

tal. mp 60—61 °C. ^{1}H-NMR ($CDCl_3$) δ: 2.23 (3H, d, J=3.9 Hz), 3.77 (2H, s), 7.12—7.16 (2H, m), 7.21—7.33 (3H, m). ^{19}F-NMR ($CDCl_3$) δ: −63.3—−63.2 (2F, m), −53.9—−53.8 (4F, m), −59.0—−58.8 (8F, m), −55.4 (1F, bs), −50.2—−50.1 (2F, m), −17.9 (3F, t, J = 9.9 Hz). IR (neat) cm^{-1}: 1702, 1226, 1148. MS *m/z*: 646 (M^+); HR-MS Calcd for $C_{20}H_{10}F_{20}O$: 646.041 (M^+), Found: 646.042 (M^+).

(*E*)-3-Benzyl-3-(trifluoromethyl)non-5-en-2-one (**5i**): Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=7.4 Hz), 1.36 (2H, sex, J=7.4 Hz), 1.97 (2H, q, J=7.4 Hz), 2.25 (3H, q, J=1.0 Hz), 2.44 (1H, dd, J=13.0, 7.3 Hz), 2.57 (1H, dd, J=13.0, 6.8 Hz), 3.02 (1H, d, J=14.0 Hz), 3.18 (1H, d, J=14.0 Hz), 5.30 (1H, m), 5.52 (1H, m), 7.12—7.16 (2H, m), 7.20—7.29 (3H, m). ^{13}C-NMR ($CDCl_3$) δ: 203.2, 135.6, 135.1, 130.5, 128.1, 127.0, 126.7 (q, J=284.5 Hz), 122.9, 62.1 (q, J=21.2 Hz), 37.8—37.9 (m), 35.5—35.6 (m), 34.6, 28.8—28.9 (m), 22.4, 13.6. ^{19}F-NMR ($CDCl_3$) δ: −1.90 (3F, s). IR (neat) cm^{-1}: 3044, 2968, 2936, 2880, 1722, 1164. MS *m/z*: 298 (M^+); HR-MS Calcd for $C_{17}H_{21}F_3O$: 298.154 (M^+), Found: 298.154 (M^+).

3-Benzyl-3-trifluoromethyl-5-methylhex-5-en-2-one (**5j**): Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.66 (3H, s), 2.29 (3H, q, J=1.4 Hz), 2.51 (1H, d, J=14.6 Hz), 2.68 (1H, d, J=14.6 Hz), 2.99 (1H, d, J=14.2 Hz), 3.25 (1H, d, J=14.2 Hz), 4.75 (1H, s), 4.91 (1H, s), 7.12—7.16 (2H, m), 7.20—7.26 (3H, m). ^{13}C-NMR ($CDCl_3$) δ: 203.3, 139.8, 135.0, 130.6, 127.9, 126.9, 126.6 (q, J=284.9 Hz), 61.9 (q, J=22.0 Hz), 40.3—40.4 (m), 38.7—38.8 (m), 28.9—29.0 (m), 23.9. ^{19}F-NMR ($CDCl_3$) δ: −1.75 (3F, s). IR (neat) cm^{-1}: 3092, 3044, 2940, 1718, 1158. MS *m/z*: 270 (M^+); HR-MS Calcd for $C_{15}H_{17}F_3O$: 270.123 (M^+), Found: 270.123 (M^+).

(*E*)-3-Benzyl-3-(trifluoromethyl)hept-5-en-2-one (**5k**): Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.66 (3H, dd, J=6.6, 1.2 Hz), 2.25 (3H, q, J=2.0 Hz), 2.43 (1H, dd, J=14.6, 7.4 Hz), 2.57 (1H, dd, J=14.6, 6.4 Hz), 3.02 (1H, d, J=14.1 Hz), 3.18 (1H, d, J=14.1 Hz), 5.32 (1H, m), 5.54 (1H, m), 7.11—7.16 (2H, m), 7.20—7.29 (3H, m). ^{13}C-NMR ($CDCl_3$) δ: 203.2, 135.0, 130.5, 130.1, 128.1, 126.9, 126.7 (q, J=286.1 Hz), 123.9, 62.0 (q, J=21.1 Hz), 37.7—37.8 (m), 35.4—35.5 (m), 28.7—28.8 (m), 18.0. ^{19}F-NMR ($CDCl_3$) δ: −2.03 (3F, s). IR (neat) cm^{-1}: 3044, 2944, 1720, 1185. MS *m/z*: 270 (M^+); HR-MS Calcd for $C_{15}H_{17}F_3O$: 270.123 (M^+), Found: 270.124 (M^+).

(5*E*,7*E*)-3-Benzyl-3-(trifluoromethyl)nona-5,7-dien-2-one (**5l**): Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.73 (3H, d, J=6.6 Hz), 2.26 (3H, q, J=1.5 Hz), 2.47 (1H, dd, J=12.6, 7.6 Hz), 2.63 (1H, dd, J=13.1, 7.5 Hz), 3.05 (1H, d, J=14.2 Hz), 3.17 (1H, d, J=14.2 Hz), 5.39 (1H, m), 5.63 (1H, m), 5.95—6.07 (2H, m), 7.10—7.15 (2H, m), 7.21—7.29 (3H, m). ^{13}C-NMR ($CDCl_3$) δ: 203.0, 134.8, 134.7, 130.9, 130.5, 129.0, 128.1, 127.1, 123.6, 126.6 (q, J=285.0 Hz), 62.1 (q, J=21.3 Hz), 37.9—38.0 (m), 35.3—35.5 (m), 25.7—25.8 (m). ^{19}F-NMR ($CDCl_3$) δ: −2.03 (3F, s). IR (neat) cm^{-1}: 3036, 2940, 1720, 1166. MS *m/z*: 296 (M^+); HR-MS Calcd for $C_{17}H_{19}F_3O$: 296.139 (M^+), Found: 296.138 (M^+).

(*E*)-3-Benzyl-3-(trifluoromethyl)-6-phenylhex-5-en-2-one (**5m**): Yellow oil. ^{1}H-NMR ($CDCl_3$) δ: 2.31 (3H, q, J=1.4 Hz), 2.61 (1H, dd, J=14.7, 7.7 Hz), 2.81 (1H, dd, J=14.7, 6.8 Hz), 3.13 (1H, d, J=14.1 Hz), 3.21 (1H, d, J=14.1 Hz), 6.06 (1H, m), 6.43 (1H, d, J=15.2 Hz), 7.13—7.32 (10H, m). ^{13}C-NMR ($CDCl_3$) δ: 202.9, 137.7, 145.5, 134.1, 130.4, 128.4, 128.2, 127.4, 127.2, 126.6 (q, J=284.8 Hz), 126.1, 123.2, 62.1 (q, J=21.2 Hz), 38.1—38.2 (m), 35.5—35.6 (m), 28.7—28.8 (m). ^{19}F-NMR ($CDCl_3$) δ: −2.05 (3F, s). IR (neat) cm^{-1}: 3040, 2936, 1720, 1168. MS *m/z*: 332 (M^+); HR-MS Calcd for $C_{20}H_{19}F_3O$: 332.139 (M^+), Found: 332.139 (M^+).

Acknowledgments This work was partially supported by Pfizer Award in Synthetic Organic Chemistry, Japan. We gratefully acknowledge to TOSOH F-TECH, Inc., for generous gift of CF_3I.

References

1) "Chemistry of Organic Fluorine Compounds II: A Critical Review," ed. by Hudlický M., Pavlath A. E., ACS Publications Division, Washington, D.C., 1995.
2) "Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications," ed. by Filler R., Kobayashi Y., Yagupolskii L. M., Elsevier, Amsterdam, 1993.
3) Welch J. T., *Tetrahedron*, **43**, 3123—3197 (1987).
4) Uneyama K., "Organofluorine Chemistry," Blackwell Publishing, Oxford, 2006.
5) "Fluorine-Containing Synthons," ed. by Soloshonok V. A., ACS symposium series 911, ACS Publications Division and Oxford University Press, Washington, D.C., 2005.
6) Tozer M. J., Herpin T. F., *Tetrahedron*, **52**, 8619—8683 (1996).
7) "Quaternary Stereocenters: Challenges and Solutions for Organic Synthesis," ed. by Christoffers J., Baro A., Wiley-VCH, Weinheim, 2005.
8) Denissova I., Barriault L., *Tetrahedron*, **59**, 10105—10146 (2003).
9) "Catalytic Asymmetric Synthesis," ed. by Ojima I., John Wiley & Sons Inc., New York, 2000.
10) Corey E. J., Guzman-Perez A., *Angew. Chem., Int. Ed.*, **37**, 388—401 (1998).
11) Kimura M., Yamazaki T., Kitazume T., Kubota T., *Org. Lett.*, **6**, 4651—4654 (2004).
12) Yamauchi Y., Kawate T., Itahashi H., Katagiri T., Uneyama K., *Tetrahedron Lett.*, **2003**, 6319—6322 (2003).
13) Hiraoka S., Yamazaki T., Kitazume T., *Chem. Commun.*, **1997**, 1497—1498 (1997).
14) Fuchigami T., Nakagawa Y., *J. Org. Chem.*, **52**, 5276—5277 (1987).
15) Ishikawa N., Yokozawa T., *Bull. Chem. Soc. Jpn.*, **56**, 724—726 (1983).
16) Sato K., Omote M., Ando A., Kumadaki I., *Org. Synth.*, **83**, 177—183 (2006).
17) Sato K., Omote M., Ando A., Kumadaki I., *Org. Lett.*, **6**, 4359—4361 (2004).
18) Sato K., Ishida Y., Murata E., Oida Y., Mori Y., Okawa M., Iwase K., Tarui A., Omote M., Kumadaki I., Ando A., submitted.
19) Tominaga T., Nishi K., Kitazume T., *J. Fluorine Chem.*, **125**, 67—71 (2004).
20) Komatsu Y., Sakamoto T., Kitazume T., *J. Org. Chem.*, **64**, 8369—8373 (1999).
21) Konno T., Kanda M., Ishihara T., Yamanaka H., *J. Fluorine Chem.*, **126**, 1517—1523 (2005).
22) Tsuji J., "Palladium Reagents and Catalysts: Innovations in Organic Synthesis," John Wiley & Sons Inc., West Sussex, 1995.