Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
Tetrahedron 62 (2006) 7199–7203

Radical trifluoromethylation of ketone Li enolates

Yoshimitsu Itoh and Koichi Mikami*

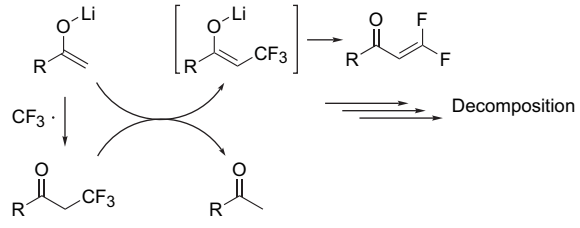
Department of Applied Chemistry, Graduate School of Science and Engineering, Tokyo Institute of Technology, 2-12-1 O-okayama, Meguro-ku, Tokyo 152-8552, Japan

Received 1 December 2005; revised 28 March 2006; accepted 30 March 2006
Available online 9 May 2006

Abstract—It has generally been believed that highly basic Li enolates cannot be applied as substrates for radical trifluoromethylation due to defluorination of the α-CF_3 product. However, Li enolates can be in fact employed for radical trifluoromethylation. Moreover, the reaction is extremely fast and the minimum reaction time is only ∼1 s.

1. Introduction

CF_3 units could make a significant functional modification of an organic molecule as a new material and medicine.[1] In recent years, we have been engaged in exploring the synthetic potential of α-CF_3 carbonyl compounds as a new building block for CF_3 containing organic compounds.[2] The α-CF_3 carbonyl compounds are sensitive to basic conditions and facile defluorination is always a problem in the synthesis (Scheme 1). Only several synthetic methodologies for introducing CF_3 unit to α-position of carbonyl group have been developed.[2d,e,3–7] We have already reported the radical trifluoromethylation of Li[2e] enolates. Further exploration of this reaction is herein reported.

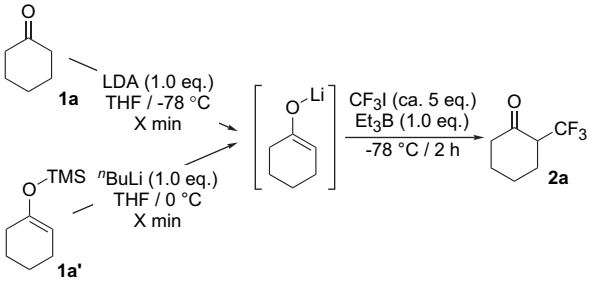


Scheme 1.

2. Results and discussion

There are two methods for the preparation of the Li enolate. One is the reaction of ketone with LDA at −78 °C and the other is the reaction of silyl enol ether with ^{n}BuLi at 0 °C (silyl-to-lithium method).[8] The former method could generate kinetic Li enolate and the latter could afford both kinetic and thermodynamic enolates depending on the parent silyl enol ether. The effect of the preparation time of the Li enolate was first investigated (Table 1). In the case of LDA method, 60 min of preparation time was necessary to give sufficient yield of the α-CF_3 product (entry 3). However, longer preparation time (120 min) was not necessary (entry 4). Without radical initiator Et_3B (entry 2), no product was detected and a large amount of cyclohexanone was recovered, indicating the radical reaction mechanism. On the other hand, in the case of silyl-to-lithium transmetallation method,

Table 1. Preparation time of the Li enolate



Entry	Substrate	*X* (min)	Yield (%)[a]
1	**1a**	30	63
2[b]		30	0
3		60	73
4		120	72
5	**1a′**	15	77
6		30	77
7		60	74
8		120	74

[a] Determined by ^{19}F NMR using BTF as an internal standard.
[b] The reaction was carried out without Et_3B.

Keywords: Trifluoromethylation; Li enolate; Radical addition.
* Corresponding author. Tel.: +81 3 5734 2142; fax: +81 3 5734 2776; e-mail: kmikami@o.cc.titech.ac.jp

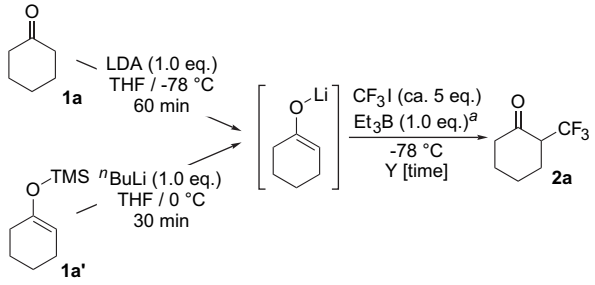
0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.03.115

the yields of the α-CF_3 product did not change over the preparation time investigated (entries 5–8, 15–120 min). This indicates that silyl-to-lithium transmetallation is completed within 15 min. However, 30 min was adopted to ensure that the transmetallation was completed.

Next, radical reaction time was investigated (Table 2). In the case of Li enolate prepared by the LDA method, 1 h of reaction time gave the product in 80% yield (entry 3). The yield decreased when the reaction was carried out for 13 h (entry 1, 62% yield), probably due to the decomposition of the α-CF_3 product when the product was exposed to basic condition for prolonged time. However, shorter reaction time did not affect the yield; found to be 'long' ~1 s is enough to give the α-CF_3 product in 81% yield (entry 5).[9] On the other hand, with Li enolate prepared by silyl-to-lithium transmetallation method, the maximum yield was given at 2 h reaction time (entry 7, 77%). Shorter reaction time decreases the yield and ~1 s reaction time gave only 34% of the α-CF_3 product (entry 9). In order to make the reaction condition almost the same as that for LDA method, the reaction was carried out in the presence of LDA (entry 10). However, LDA did not affect the reaction. The difference between these two methods is not clear. However, it can be said that 2 h of reaction time is required for silyl-to-lithium method.

A variety of ketonic substrates were investigated using LDA to generate Li enolate (Table 3). In the case of cyclohexanone (entry 1) and 4-^{t}Bu- (entry 2), 2-Me- (entry 3), and 2-Ph- (entry 4) cyclohexanones, the reactions proceeded with extremely fast reaction rates and provided the α-CF_3 products in fair to good yields. The reaction rates of cyclopentanone (entry 5) and cycloheptanone (entry 6) were relatively slow (5 min). For acyclic substrates (entries 7–9), the yields were poor. Ester and amide were also investigated but did not give the α-CF_3 product at all. From the results described above, cyclohexanone derivatives are the most suitable substrate for this reaction system.

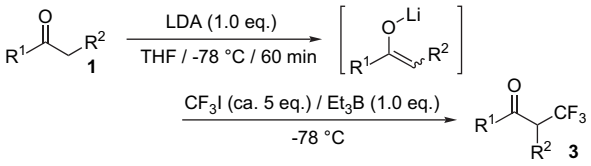
Table 2. Investigation of the trifluoromethylation time



Entry	Substrate	Reaction time Y	Yield (%)[b]
1	**1a**	13 h	62
2		2 h	73
3		1 h	80
4		1 min	83
5		~1 s	81
6	**1a′**	13 h	52
7		2 h	77
8		30 min	67
9		~1 s	34
10[c]		~1 s	36

[a] Et_3B was added in flat 15 s.
[b] Determined by ^{19}F NMR using BTF as an internal standard.
[c] In the presence of LDA.

Table 3. Radical trifluoromethylation of Li enolates prepared by LDA method



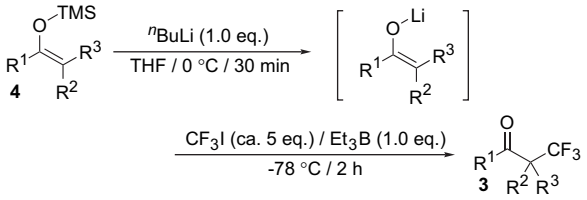
Entry[a]	Substrate	Product	Reaction time	Yield (%)[b]
1	**1a**	**2a**	~1 s	81
2	**1b**	**2b**	~1 s	71 (67) [73:27]
3	**1c**	**2c**	~1 s	74 [57:43]
4	**1d**	**2d**	~1 s	43 (40) [57:43]
5	**1e**	**2e**	5 min	40
6	**1f**	**2f**	5 min	48
7	**1g**	**2g**	5 min	25
8	**1h**	**2h**	5 min	17
9	**1i**	**2i**	1 min	35

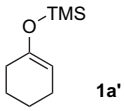
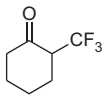
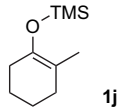
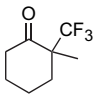
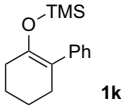
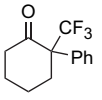
[a] Et_3B was added in flat 15 s.
[b] Determined by ^{19}F NMR using BTF as an internal standard. The values in ( ) refer to the yields of isolated products. The values in [ ] are the diastereomeric ratio.

Li enolates prepared by silyl-to-lithium transmetallation method were also investigated for the most suitable cyclohexanone derivatives (Table 4). α-Me- and α-Ph-cyclohexanones provided the products, which bear quaternary carbon centers attached with CF_3, in fair yields (entries 2 and 3).

In view of asymmetric radical trifluoromethylation, several solvents and additives were examined (Table 5). α-Ph-cyclohexanone was adopted as the substrate in order to prevent the racemization of the product. The parent Li enolate was generated by silyl-to-lithium method in the presence of DME or TMEDA. In THF, addition of DME (entry 2) and TMEDA

Table 4. Radical trifluoromethylation of Li enolates prepared by silyl-to-lithium method

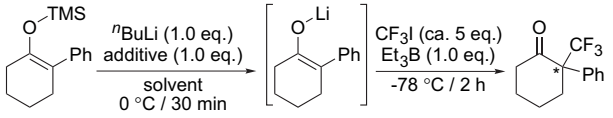


Entry[a]	Substrate	Product	Yield (%)[b]
1	 **1a'**	 **2a**	77
2[c]	 **1j**	 **2j**	58
3[d]	 **1k**	 **2k**	44 (45)

[a] Et$_3$B was added in flat 15 s.
[b] Determined by ^{19}F NMR using BTF as an internal standard. The values in ( ) refer to the yields of isolated products.
[c] Silyl enol ether of α-Me-cyclohexanone consists of thermodynamic and kinetic enol ethers (87:13).
[d] Silyl enol ether of α-Ph-cyclohexanone consists only thermodynamic enol ether.

(entry 3) made no significant effect. When the reaction was carried out in Et_2O solution, the α-CF_3 product was obtained only in 11% (entry 4). The reaction was accelerated by DME (entry 5, 34% yield) or TMEDA (entry 6, 26% yield) in Et_2O solution. The product was obtained only when the TMEDA was added though in only 9% (entry 9) in $^iPr_2O$ solution. The reaction was also accelerated in ^{t}BuOMe solution. The yield was 5% without additive. Addition of DME (entry 11) and TMEDA (entry 12) increased the yield to 15 and 18%, respectively. When the reaction was carried out with 1.0 equiv of (*S*,*S*)-hydrobenzoin dimethyl ether in Et_2O, the product was obtained in 39% yield with 27% ee. In ^{t}BuOMe solution, the reaction with (−)-sparteine gave the product in 13% yield with −44% ee. These results show the possibility of catalytic asymmetric radical trifluoromethylation of enolates.

Table 5. Effect of the bidentate additive



Entry	Solvent	Additive	Yield (%)
1	THF	—	45[a]
2		DME	38[a]
3		TMEDA	34[a]
4	Et_2O	—	11[b]
5		DME	34[a]
6		TMEDA	26[a]
7	$^iPr_2O$	—	—
8		DME	—
9		TMEDA	9[b]
10	^{t}BuMeO	—	5[b]
11		DME	15[b]
12		TMEDA	18[b]

[a] Yield of the isolated products.
[b] Determined by ^{19}F NMR using BTF as an internal standard.

In summary, we have discovered that highly basic Li enolates can be employed for radical trifluoromethylation. The reaction rate is extremely fast compared to the previous radical trifluoromethylation. The direct use of Li enolates is simpler and faster than that of Ti ate enolates or any other previous enolate equivalents.

3. Experimental

3.1. General

^{1}H NMR and ^{13}C NMR were measured on Varian Gemini 2000 (300 MHz) spectrometer and ^{19}F NMR was measured on Varian UNITY INOVA (400 MHz) spectrometer. Chemical shifts of ^{1}H NMR were expressed in parts per million downfield from tetramethylsilane as an internal standard (δ=0) in $CDCl_3$. Chemical shifts of ^{13}C NMR were expressed in parts per million downfield from $CDCl_3$ as an internal standard (δ=77.0) in $CDCl_3$. Chemical shifts of ^{19}F NMR were expressed in parts per million downfield from BTF as an internal standard (δ=−63.24) in $CDCl_3$. IR spectra were measured on JASCO FT/IR-5000 spectrometer. EI mass spectra were measured on Shimadzu QP-5000 spectrometer. Analytical thin layer chromatography (TLC) was performed on glass plates and/or aluminum sheets pre-coated with silica gel (Merck Kieselgal 60 F254, layer thickness 0.25 and 0.2 mm). Visualization was accomplished by UV light (254 nm), anisaldehyde, $KMnO_4$, and phosphomolybdic acid. Column chromatography was performed on Merck Kieselgel 60 and KANTO Silica Gel 60N (spherical, neutral), employing hexane ethyl acetate mixture as an eluent unless otherwise noted. THF was distilled from benzophenone-ketyl under Ar prior to use. All experiments were carried out under argon atmosphere unless otherwise noted.

3.2. General procedure: starting from ketone

To a solution of $^iPr_2NH$ (28.0 μl, 0.20 mmol) in THF (2.0 ml) was added ^{n}BuLi (126.3 μl of 1.58 M solution in hexane, 0.20 mmol) at −78 °C. The reaction mixture was stirred at 0 °C for 30 min and then cooled to −78 °C. To the solution was added cyclohexanone (20.7 μl, 0.2 mmol) and the solution was stirred for 60 min at the temperature. Then, gaseous CF_3I (ca. 200 mg, ca. 1.0 mmol) was added with a cannula. Next, a syringe, which was filled with 0.12 ml of 5 M solution of acetic acid in THF, was set to the reaction vessel and kept untouched till quenching the reaction. Then Et_3B (0.2 ml of 1.0 M solution in hexane, 0.2 mmol) was added in flat 15 s to start the radical addition reaction. The reaction mixture was immediately quenched (in ∼1 s) by acetic acid solution, which was set beforehand, at −78 °C. After warming to room temperature, BTF (10 μl, 0.082 mmol) was added as an internal standard. The yield was determined by ^{19}F NMR of the crude mixture (81%).

3.3. General procedure: starting from silyl enol ether

To a solution of 1-(trimethylsilyloxy)cyclohexene (38.9 μl, 0.2 mmol) in THF was added ^{n}BuLi (128.2 μl of 1.56 M solution in hexane, 0.20 mmol) at 0 °C and stirred for 30 min at the temperature. Then, the reaction mixture was cooled to −78 °C. To the mixture was added gaseous CF_3I (ca. 200 mg, ca. 1.0 mmol) with a cannula followed by Et_3B (0.2 ml of 1.0 M solution in hexane, 0.2 mmol). The reaction mixture was stirred for 2 h at −78 °C and then quenched by acetic acid (0.12 ml of 5 M solution in THF) at −78 °C. After warming to room temperature, BTF (10 μl, 0.082 mmol) was added as an internal standard. The yield was determined by ^{19}F NMR of the crude mixture (77%).

3.4. 2-Trifluoromethyl-cyclohexanone (2a)

^{1}H NMR ($CDCl_3$): δ 1.62–1.88 (m, 3H), 1.92–2.14 (m, 2H), 2.24–2.39 (m, 2H), 2.42–2.53 (m, 1H), 2.98–3.13 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 23.7, 27.1, 27.5 (q, *J*=2.4 Hz), 42.2, 53.6 (q, *J*=25.7 Hz), 124.6 (q, *J*=279.5 Hz), 203.0. ^{19}F NMR ($CDCl_3$): δ −69.3 (d, 7.9 Hz). IR (neat): 2954, 2876, 2364, 1729, 1272, 1170, 1125, 1060 cm^{-1}. EI-MS *m*/*z*: 166 [M$^{+\bullet}$].

3.5. 4-Tertiarybutyl-2-trifluoromethyl-cyclohexanone (2b)

Major isomer: ^{1}H NMR ($CDCl_3$): δ 0.94 (s, 9H), 1.42–1.68 (m, 3H), 2.18–2.20 (m, 1H), 2.26–2.42 (m, 2H), 2.44–2.56 (m, 1H), 3.00–3.16 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 27.5, 28.1, 28.6, 32.5, 41.7, 46.1, 53.0 (q, *J*=25.7 Hz), 124.6 (q, *J*=279.6 Hz), 203.2. ^{19}F NMR ($CDCl_3$): δ −69.7 (d, *J*=7.9 Hz). IR (KBr): 2970, 2878, 1734, 1392, 1369, 1274, 1170, 1120, 1067 cm^{-1}. EI-MS *m*/*z*: 222 [M$^{+\bullet}$]. Minor isomer (isomerization was observed during isolation. Therefore, only ^{19}F NMR data could be shown): ^{19}F NMR ($CDCl_3$): δ −66.1 (d, *J*=10.5 Hz).

3.6. 2-Methyl-6-trifluoromethyl-cyclohexanone (2c)

Major isomer: ^{1}H NMR ($CDCl_3$): δ 1.03 (d, *J*=6.3 Hz, 3H), 1.34–1.49 (m, 1H), 1.63–1.87 (m, 2H), 1.88–2.03 (m, 1H), 2.08–2.19 (m, 1H), 2.30–2.49 (m, 2H), 2.98–3.16 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 13.8, 24.0, 28.3, 36.3, 45.9, 53.7 (q, *J*=25.7 Hz), 124.8 (q, *J*=279.5 Hz), 204.6. ^{19}F NMR ($CDCl_3$): δ −69.8 (d, *J*=8.3 Hz). IR (neat): 2942, 2874, 2366, 1731, 1456, 1392, 1332, 1272, 1170, 1137, 1123, 1038, 832, 688 cm^{-1}. EI-MS *m*/*z*: 180 [M$^{+\bullet}$]. Minor isomer: ^{1}H NMR ($CDCl_3$): δ 1.11 (d, *J*=6.6 Hz, 3H), 1.46–2.21 (m, 6H), 2.57–2.71 (m, 1H), 3.07–3.22 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 15.0, 20.2, 26.9, 29.6, 34.2, 44.5, 52.3 (q, *J*=25.7 Hz), 125.2 (q, *J*=280.7 Hz), 206.3. ^{19}F NMR ($CDCl_3$): δ −66.7 (d, *J*=10.2 Hz). IR (neat): 2928, 2858, 2364, 2344, 1725, 1458, 1265, 1143, 801 cm^{-1}. EI-MS *m*/*z*: 180 [M$^{+\bullet}$].

3.7. 2-Phenyl-6-trifluoromethyl-cyclohexanone (2d)

Major isomer: ^{1}H NMR ($CDCl_3$): δ 1.83–2.21 (m, 4H), 2.28–2.40 (m, 1H), 2.40–2.56 (m, 1H), 3.16–3.35 (m, 1H), 3.56–3.68 (dd, *J*=5.4, 12.6 Hz, 1H), 7.11–7.17 (m, 2H), 7.25–7.40 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 24.2, 28.3, 35.6, 54.1 (q, *J*=25.6 Hz), 57.8, 124.6 (q, *J*=280.8 Hz), 127.4, 128.4, 128.8, 137.0, 201.6. ^{19}F NMR ($CDCl_3$): δ −69.6 (d, *J*=7.9 Hz). IR (KBr): 3036, 2946, 2872, 1722, 1605, 1452, 1385, 1270, 1168, 1133, 1045, 761, 704, 592 cm^{-1}. EI-MS *m*/*z*: 242 [M$^{+\bullet}$]. Minor isomer: ^{1}H NMR ($CDCl_3$): δ 1.86–2.28 (m, 5H), 2.37–2.52 (m, 1H), 3.12–3.30 (dq, *J*=6.0, 9.3 Hz, 1H), 3.82–3.92 (distorted t, *J*=6.3 Hz, 1H), 7.17–7.43 (m, 5H). ^{13}C NMR ($CDCl_3$): δ 20.4, 27.4, 31.3, 52.0 (q, *J*=26.9 Hz), 55.1, 125.1 (q, *J*=280.8 Hz), 127.4, 127.6, 129.0, 136.7, 203.5. ^{19}F NMR ($CDCl_3$): δ −67.9 (d, *J*=9.0 Hz). IR (neat): 3066, 3032, 2954, 2878, 2364, 1725, 1603, 1584, 1499, 1454, 1390, 1332, 1274, 1183, 1141, 698 cm^{-1}. EI-MS *m*/*z*: 242 [M$^{+\bullet}$].

3.8. 2-Trifluoromethyl-cyclopentanone (2e)

^{1}H NMR ($CDCl_3$): δ 1.77–2.00 (m, 1H), 2.01–2.21 (m, 2H), 2.22–2.48 (m, 3H), 2.78–2.97 (qm, *J*=9.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 20.0, 24.4, 38.5, 51.1 (q, *J*=26.9 Hz), 124.6 (q, *J*=278.3 Hz), 209.4. ^{19}F NMR ($CDCl_3$): δ −67.9 (d, *J*=10.5 Hz). IR (neat): 2986, 2896, 2366, 2344, 1758, 1638, 1367, 1313, 1257, 1187, 1151, 1096, 1046 cm^{-1}. EI-MS *m*/*z*: 152 [M$^{+\bullet}$].

3.9. 2-Trifluoromethyl-cycloheptanone (2f)

^{1}H NMR ($CDCl_3$): δ 1.22–1.48 (m, 2H), 1.48–1.75 (m, 2H), 1.86–2.05 (m, 3H), 2.09–2.20 (m, 1H), 2.54–2.61 (m, 2H), 3.16–3.31 (qdd, *J*=4.1, 8.9, 11.1 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 24.4, 24.7 (q, *J*=2.4 Hz), 27.5, 29.1, 43.1, 55.5 (q, *J*=24.5 Hz), 124.9 (q, *J*=280.8 Hz), 205.9. ^{19}F NMR ($CDCl_3$): δ −69.0 (d, 9.0 Hz). IR (neat): 2940, 2866, 1721, 1178, 1151, 1096 cm^{-1}. EI-MS *m*/*z*: 180 [M$^{+\bullet}$].

3.10. 1,1,1-Trifluoro-5-phenyl-3-pentanone (2g)

^{1}H NMR ($CDCl_3$): δ 2.80–3.00 (m, 4H), 3.19 (q, *J*=10.2 Hz, 2H), 7.14–7.35 (m, 5H). ^{13}C NMR ($CDCl_3$): δ 29.2, 44.9, 46.5 (q, *J*=28.1 Hz), 123.5 (q, *J*=277.1 Hz), 126.4, 128.3, 128.6, 140.1, 199.1. ^{19}F NMR ($CDCl_3$): δ −62.9 (t, *J*=10.2 Hz). IR (neat): 3068, 3032, 2922, 1734, 1605, 1497, 1456, 1419, 1377, 1261, 1154, 1096, 750, 700 cm^{-1}. EI-MS *m*/*z*: 216 [M$^{+\bullet}$].

3.11. 1,1,1-Trifluoro-4,4-dimethyl-5-phenyl-3-pentanone (2h)

^{1}H NMR ($CDCl_3$): δ 1.16 (s, 6H), 2.81 (s, 2H), 3.17 (q, *J*=9.9 Hz, 2H), 7.07 (ddd, *J*=1.7, 2.1, 6.3 Hz, 2H), 7.19–7.32 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 23.8, 41.4 (q, *J*=28.1 Hz), 45.3, 48.9, 123.9 (q, *J*=277.1 Hz), 126.8, 128.2, 130.2, 136.8, 205.2. ^{19}F NMR ($CDCl_3$): δ −63.0 (t, *J*=9.8 Hz). IR (neat): 3034, 2976, 1721, 1369, 1282, 1133, 1100 cm^{-1}. EI-MS *m*/*z*: 244 [M$^{+\bullet}$].

3.12. 7-Trifluoromethyl-6-undecanone (2i)

^{1}H NMR ($CDCl_3$): δ 0.90 (t, *J*=3.9 Hz, 6H), 1.18–1.41 (m, 8H), 1.53–1.65 (m, 2H), 1.65–1.79 (m, 1H), 1.81–1.97 (m, 1H), 2.47 (dt, *J*=18.0, 7.2 Hz, 1H), 2.61 (dt, *J*=7.4, 18.0 Hz, 1H), 3.11–3.26 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 13.6, 13.8, 22.4, 22.7, 25.59, 25.62, 29.0, 31.1, 43.6, 55.6 (q, *J*=24.4 Hz), 124.9 (q, *J*=280.7 Hz), 204.5. ^{19}F NMR ($CDCl_3$): δ 67.4 (d, *J*=9.0 Hz). IR (neat): 2966, 2938, 2870, 1731, 1263, 1164 cm^{-1}. EI-MS *m*/*z*: 238 [M$^{+\bullet}$].

3.13. 2-Methyl-2-trifluoromethyl-cyclohexanone (2j)

^{1}H NMR ($CDCl_3$): δ 1.36 (s, 3H), 1.70–2.00 (m, 5H), 2.06–2.20 (m, 1H), 2.35–2.58 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 17.7 (q, J=2.4 Hz), 20.5, 26.4, 33.5, 39.4, 53.7 (q, J=23.2 Hz), 126.5 (q, J=283.2 Hz), 206.2. ^{19}F NMR ($CDCl_3$): δ −73.6 (s). IR (neat): 2936, 2874, 1725, 1274, 1170, 1137 cm^{-1}. EI-MS m/z: 180 [M$^{+\bullet}$].

3.14. 2-Phenyl-2-trifluoromethyl-cyclohexanone (2k)

^{1}H NMR ($CDCl_3$): δ 1.63–1.86 (m, 3H), 1.89–2.00 (m, 1H), 2.12–2.25 (m, 1H), 2.31–2.40 (m, 2H), 2.91 (qd, J=3.0, 14.4 Hz, 1H), 7.29–7.35 (m, 2H), 7.35–7.47 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 20.2, 27.4, 29.9 (q, J=2.4 Hz), 39.8, 62.2 (q, J=22.0 Hz), 125.1 (q, J=283.2 Hz), 128.7, 128.8, 129.0, 131.8, 204.7. ^{19}F NMR ($CDCl_3$): δ −72.9 (s). IR (neat): 3066, 2954, 2874, 1725, 1282, 1255, 1176, 1152 cm^{-1}. EI-MS m/z: 242 [M$^{+\bullet}$].

References and notes

1. (a) Ma, J.-A.; Cahard, D. *Chem. Rev.* **2004**, *104*, 6119–6146; (b) Mikami, K.; Itoh, Y.; Yamanaka, M. *Chem. Rev.* **2004**, *104*, 1–16; (c) Hiyama, T.; Kanie, K.; Kusumoto, T.; Morizawa, Y.; Shimizu, M. *Organofluorine Compounds*; Springer: Berlin, Heidelberg, 2000; (d) *Enantiocontrolled Synthesis of Fluoro-Organic Compounds*; Soloshonok, V. A., Ed.; Wiley: Chichester, UK, 1999; (e) *Asymmetric Fluoroorganic Chemistry, Synthesis, Applications, and Future Directions*; Ramachandran, P. V., Ed.; American Chemical Society: Washington, DC, 2000; (f) *Organofluorine Chemistry*; Chambers, R. D., Ed.; Springer: Berlin, 1997; (g) Iseki, K. *Tetrahedron* **1998**, *54*, 13887–13914; (h) *Biomedical Frontiers of Fluorine Chemistry*; Ojima, I., McCarthy, J. R., Welch, J. T., Eds.; American Chemical Society: Washington, DC, 1996; (i) Smart, B. E., Ed.; *Chem. Rev.* **1996**, *96*, 1555–1824 (Thematic issue of Fluorine Chemistry); (j) *Organofluorine Chemistry: Principles and Commercial Applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum: New York, NY, 1994; (k) McClinton, M. A.; McClinton, D. A. *Tetrahedron* **1992**, *48*, 6555–6666; (l) Hudlicky, M. *Chemistry of Organic Fluorine Compounds*, 2nd ed. Ellis Horwood: Chichester, UK, 1976.
2. (a) Itoh, Y.; Yamanaka, M.; Mikami, K. *Org. Lett.* **2003**, *5*, 4803–4806; (b) Itoh, Y.; Yamanaka, M.; Mikami, K. *Org. Lett.* **2003**, *5*, 4807–4809; (c) Itoh, Y.; Yamanaka, M.; Mikami, K. *J. Am. Chem. Soc.* **2004**, *126*, 13174–13175; (d) Itoh, Y.; Mikami, K. *Org. Lett.* **2005**, *7*, 649–651; (e) Our preliminary report on the radical trifluoromethylation of Li enolates: Itoh, Y.; Mikami, K. *Org. Lett.* **2005**, *7*, 4883–4885.
3. Trifluoromethylation of Li enolate of hindered imides (only exception for the use of Li enolate): (a) Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron Lett.* **1993**, *34*, 2169–2170; (b) Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron: Asymmetry* **1994**, *5*, 961–974. They have succeeded in trifluoromethylation by adopting Evans oxazolidinones with bulky substituent at α-position to suppress defluorination.
4. Perfluoroalkylation of silyl and germyl enol ethers of esters and ketones: (a) Miura, K.; Taniguchi, M.; Nozaki, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1990**, *31*, 6391–6394; (b) Miura, K.; Takeyama, Y.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1542–1553. Perfluoroalkylation of silyl enol ethers provided the products in good yields except for trifluoromethylation. Trifluoromethylation of ketone germyl enol ethers proceeds in good yield.
5. Trifluoromethylation of enamines: (a) Cantacuzène, D.; Wakselman, C.; Dorme, R. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1365–1371; (b) Kitazume, T.; Ishikawa, N. *J. Am. Chem. Soc.* **1985**, *107*, 5186–5191.
6. Trifluoromethylation of enol acetates: Langlois, B. R.; Laurent, E.; Roidot, N. *Tetrahedron Lett.* **1992**, *33*, 1291–1294.
7. There are some reports of trifluoromethylation using CF_3^+: (a) Yagupol'skii, L. M.; Kondratenko, N. V.; Timofeeva, G. N. *J. Org. Chem. USSR* **1984**, *20*, 115–118; (b) Umemoto, T.; Ishihara, S. *J. Am. Chem. Soc.* **1993**, *115*, 2156–2164; (c) Umemoto, T.; Adachi, K. *J. Org. Chem.* **1994**, *59*, 5692–5699.
8. (a) Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4462–4464; (b) Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4464–4465.
9. For accuracy, Et_3B was added in flat 15 s and the reaction time was counted from the time when the addition of Et_3B was completed.