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# Reductive modification of difluoromethylene moiety in pentafluoropropionyl group

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**Abstract**

The reductive Mg-promoted defluorinative-silylation of 2,2,3,3,3-pentafluoropropiophenone readily produces the α-trifluoromethyl enol silyl ether, which then react with electrophiles to give a variety of 2-substituted-3,3,3-trifluoropropiophenones in excellent yields. The same protocol is applicable for the preparation of enol silyl ether of 3,3,3-trifluoropropiophenone. Fluoride ion catalyzed 1,2-desilylative-defluorination of 2,3,3,3-tetrafluoro-2-trimethylsilyloxypropiophenone provided 3,3,3-trifluoro-1-phenyl-1,2-propanedione in a good yield.


*Keywords:* α-Trifluoromethyl enol silyl ethers; 2-Substituted-3,3,3-trifluoropropiophenones; Reductive-defluorination; Desilylative-defluorination; Magnesium

## 1. Introduction

Development of general and efficient selective introduction of a trifluoromethyl group into organic compounds has kept high attentions in both academia and industry. This is because many commercially available pharmaceuticals and agrochemicals owe their biological activity to the unique nature of trifluoromethyl group [1–4]. α-$CF_3$ carbonyl compounds can be used as useful building blocks for attractive trifluoromethylated compounds by the functionalization of α-position and subsequent transformation of carbonyl groups [5–8]. However there are many synthetic difficulty, such as easy defluorination of the $CF_3CH_2$ anion species [9–12]. Mikami and Itoh have reported a direct aldol reaction with *in situ* generated Ti-enolate of α-$CF_3$ ketones [13–15]. Recently, it was reported that the use of metal enolates could avoid significant defluorination during radical trifluoromethylation [15–20]. Most feasible way to functionalize α-position of $CF_3$-ketones is *via* a reaction of enol silyl ethers [21–23], and in some cases, the related boron and aluminum enolates [24,25]. However, there are only a few reports which described the synthetic methods of α-$CF_3$ carbonyl compounds, which required expensive starting materials and gave low yields. For example, 3,3,3-trifluoropropiophenone is synthesized by Friedel-Crafts reaction of benzene with 3,3,3-trifluoropropionic chloride, which is rather expensive [21]. A three-steps synthesis of 3,3,3-trifluoropropiophenone *via* trifluoroacetylation of benzaldehyde dimethylhydrazone is not practical due to the low total yield [26,6,7].

Mg(0)-promoted C–F bond activation method has found useful for the transformation of trifluoromethyl ketones to 2,2-difluoroenol silyl ethers, building-blocks feasible for $CF_2$ compounds syntheses [27]. Herein, we describe a facile and reliable preparation of α-trifluoromethyl enol silyl ethers **2** and **4**, and their effective transformations to trifluoromethyl α-diketone and 2-substituted-3,3,3-trifluoropropiophenones.

## 2. Results and discussion

A series of the reductive transformations of **1**–**4** are shown in Scheme 1. Tetrafluoro enol silyl ether **2** was prepared by the Mg(0)-promoted defluorinative-silylation of **1** in an excellent yield. Hydrolysis was then followed to afford 2,3,3,3-tetrafluoropropiophenone **3** under acid catalysis. The second Mg(0)-promoted defluorinative-silylation of **3** was proceeded smoothly to afford 3,3,3-trifluoro enol silyl ether **4** in 90% yield. The above described synthesis of **4** involves high availability of **1**, mild reaction conditions and an excellent total yield in comparison with synthesis by *O*-silylation of the less available 3,3,3-trifluoropropiophenone with $Me_3SiOTf$ [21].

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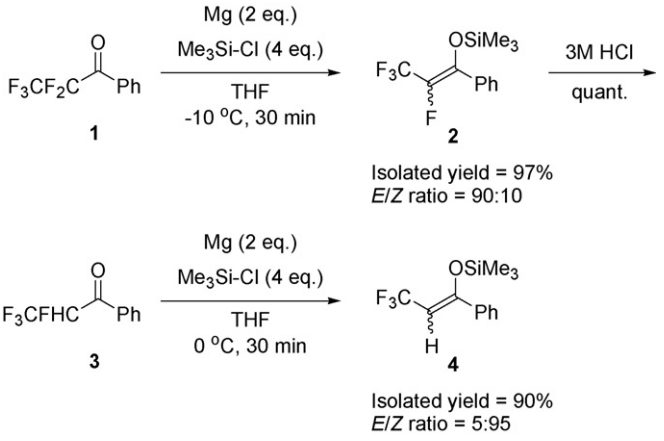


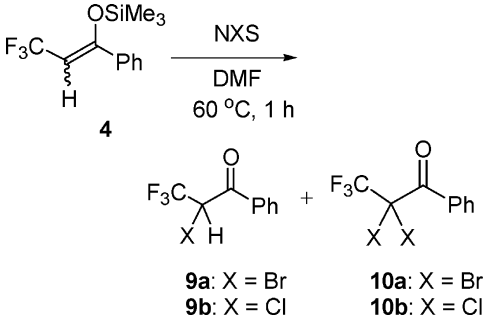

Scheme 1.

Interestingly, the relative stereochemistry of substituents $CF_3$ and $OSiMe_3$ groups in both enol silyl ethers **2** and **4** is *cis* to each other. This stereochemical preference may arise from the intramolecular C–F. . .Si coordinative interaction as suggested by Shi and co-workers [28].

Transformations of **2** and **4** to a series of 2-substituted-3,3,3-trifluoropropiophenones were examined. 2,3,3,3-Tetrafluoropropenyl silyl ether **2** reacts with *m*-chloroperbenzoic acid (*m*-CPBA) in dichloromethane to afford the 2,3,3,3-tetrafluoro-2-trimethylsiloxypropiophenone **6** (Scheme 2). It is suggested that **6** is produced by migration of trimethylsilyl group on ring opening of epoxide **5** initially formed in the oxidation step [29,30]. Following fluoride ion promoted desilylative-defluorination of **6** proceeded smoothly to provide a valuable 1,2-diketone **7** by the use of catalytic amount of fluoride ion (Scheme 3), which is recycled as demonstrated by several 1,2- [31], 1,4- [32] and 1,6-desilylative-defluorination reactions [33].

Moreover, the reaction of **2** with various electrophiles afforded the 2-substituted-2,3,3,3-tetrafluoropropiophenones **8**. Thus, halogenation and sulfenylation proceeded smoothly under the very mild conditions to give 2-chloro, 2-bromo and 2-phenylthio-2,3,3,3-tetrafluoropropiophenones **8a**–**8c** in excellent yields, respectively. Carbon–carbon bond formation at the α-carbon of **2** is also possible. In the presence of Lewis acid, the reaction of **2** with benzaldehyde dimethyl acetal gave **8d** in 95% yield (Table 1).

Table 2
Products and yields in the reaction of **4** with NXS



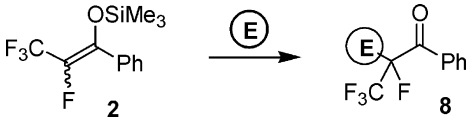

| Entry | NXS (eq.) | Yield (%)[a] | |
|---|---|---|---|
| | | **9** | **10** |
| 1 | NBS (1.1) | 99 (97) | 0 |
| 2 | NBS (2.1) | 91 | 7 |
| 3 | NCS (1.1) | 65 | 21 |
| 4 | NCS (2.1) | 0 | 99 (96) |

[a] Yields were analyzed by $^{19}F$ NMR integration of products relative to $C_6F_6$ as an internal standard. Yield in parentheses were isolated yields.

Lewis acid catalyzed alkylation of **4** was already reported [21]. Here, an interesting double chlorination is described. The reaction of **4** with NBS provided a monobromide **9a** exclusively in quantitative yield. Meanwhile, the reaction of **4** with 1.1 eq. of NCS provided a mixture of a monochloride **9b** and a dichloride **10b** in favor of **9b**. Addition of 2.1 eq. of NCS provided only the dichloride **10b** in 96% yield. It seems that α-proton of **9b** would be more acidic than **9a**, meanwhile dibromide **10a** would be thermodynamically less stable than monobromide **9a** presumably due to the steric crowd at α,α-dibromo-α-trifluoromethylated carbon of **10a** (Table 2).

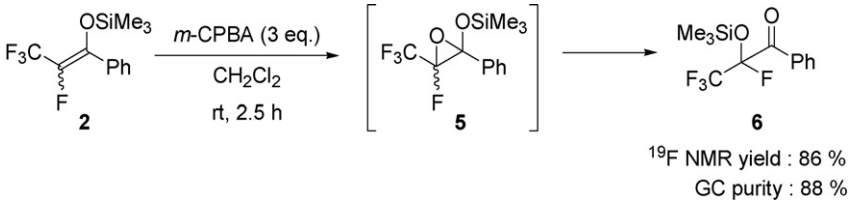
In conclusion, a variety of 2-substituted-3,3,3-trifluoropropiophenones were synthesized in high yields *via* reductive Mg(0)-promoted defluorinative-silylation of easily available 2,2,3,3,3-pentafluoropropiophenone.

Table 1
Products and yields of **8** in the reaction of **2** with electrophiles




| Entry | Electrophile | Reaction conditions | Ⓔ[a] | Product, Yield[b] (%) |
|---|---|---|---|---|
| 1 | NCS | DMF, rt, 1 h | Cl | **8a**, 97 |
| 2 | NBS | DMF, rt, 1 h | Br | **8b**, 99 |
| 3 | PhSCl | DMF, rt, 1 h | PhS | **8c**, 91 |
| 4 | $PhCH(OMe)_2$ | TMSOTf (1 eq.), $CH_2CI_2$, 0 °C, 4 h | PhCH(OMe) | **8d**, 95[c] |

[a] Substituent E in products 8.
[b] Isolated yields.
[c] Diastereomer mixture. Diastereomeric ratio was determined by $^1H$ NMR (65:35).




Scheme 2.

## 3. Experimental

### 3.1. General

$^{1}H$, $^{13}C$ and $^{19}F$ NMR spectra were recorded at 600, 150 and 564 MHz on a Varian UNITY INOVA 600 instrument, respectively. The chemical shift were reported in $\delta$ (ppm) related to the $CHCl_3$ (7.26 ppm) $CDCl_3$ (77 ppm) and $C_6F_6$ (0 ppm). Coupling constants ($J$) were reported in hertz (Hz). Infrared spectra were reported on a Hitachi 270-30 spectrometer. Only selected absorbance were reported ($\lambda$ in $cm^{-1}$). MS analyses were performed on a SHIMADZU GCMS-QP5050A. Elemental analyses were performed on a Perkin-Elmer series II CHNS/O Analyzer 2400. Melting points were determined on a Yanako MP-S3 melting point measurement apparatus. All air- or moisture-sensitive reactions were carried out under argon atmosphere with freshly distilled solvents. THF was distilled from sodium and benzophenone ketyl. DMF and $Me_3Si$–Cl were used after distillation over $CaH_2$. $CH_2Cl_2$ was freshly distilled from $P_2O_5$. *m*-CPBA was washed with phosphate buffer and distilled water, then dried under reduced pressure. The other reagents were used without further purification. Mg turnings were purchased from nacalai tesque. Tetrabutylammonium triphenyldifluorosilicate (TBAT) was purchased from Aldrich. Column chromatography was carried out on silica gel (Merck, Silica gel 60).

### 3.2. Experimental procedures

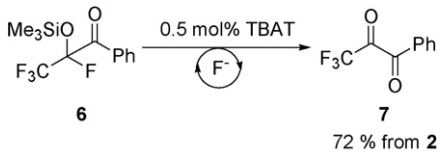
#### 3.2.1. 1-Phenyl-2,3,3,3-tetrafluoro-1-trimethylsiloxypropene (2)

A suspension of $Me_3Si$–Cl (5 mL, 40 mmol) in distilled THF (40 mL) and Mg (turnings) (0.49 g, 20 mmol) was cooled down at −10 °C under argon atmosphere. 2,2,3,3,3-Pentafluoropropiophenone **1** (2.24 g, 10 mmol) was added dropwise and then the mixture was stirred for 20 min. Then, 1,4-dioxane (5 mL) was added to the reaction mixture, and stirred for 5 min at −10 °C. Residual magnesium and dioxane–$MgCl_2$ salt were separated by filtration through completely dried Celite. THF, $Me_3Si$–Cl and 1,4-dioxane were removed under reduced pressure, and *n*-hexane was added. The resulting salt was removed by filtration through completely dried Celite. Evaporation of filtrate and distillation (0.5 mmHg, 50 °C) provided a colorless oil of **2** (2.70 g, 97%) as a mixture of *E*/*Z* isomers (90:10 by $^{19}F$ NMR). IR (neat): 2968, 1680, 1378, 1276, 1186, 862 $cm^{-1}$; $^{1}H$ NMR (600 MHz, $CDCl_3$): (*E* isomer) $\delta$ 0.09 (9H, s, $Me_3Si$), 7.37–7.43 (3H, m), 7.52–7.54 (2H, m), (*Z* isomer) $\delta$ 0.16 (9H, s, $Me_3Si$), 7.37–7.43 (3H, m), 7.52–7.54 (2H, m); $^{13}C$ NMR (150 MHz, $CDCl_3$): (*E* isomer) $\delta$ 0.06 ($Me_3Si$), 120.4 (dq, $J$ = 37, 270 Hz, $CF_3$), 137.8 (dq, $J$ = 239, 37 Hz), 143.2 (dq, $J$ = 30, 3 Hz), (*Z* isomer) $\delta$ 0.25 ($Me_3Si$), 120.5 (dq, $J$ = 37, 270 Hz, $CF_3$), 135.8 (dq, $J$ = 240, 39 Hz), 142.5 (dq, $J$ = 30, 3 Hz); $^{19}F$ NMR (564 MHz, $CDCl_3$): (*E* isomer) $\delta$ −4.6 (1F, q, $J$ = 11 Hz), 96.1 (3F, d, $J$ = 11 Hz, $CF_3$), (*Z* isomer) $\delta$ 7.8 (1F, q, $J$ = 13 Hz), 97.8 (3F, d, $J$ = 13 Hz, $CF_3$); EI MS *m*/*z* (relative intensity): 278 $[M]^+$ (15), 263 $[M–Me]^+$ (5), 186 $[M-92]^+$ (13), 177 $[M-101]^+$ (20), 139 $[M-139]^+$ (18), 105 $[M-173]^+$ (43), 77 $[Ph]^+$ (100), 73 $[Me_3Si]^+$ (91); Anal. Calcd for $C_{12}H_{14}F_4OSi$: C, 51.79; H, 5.07. Found: C, 51.59; H, 5.13.

The stereochemistry of the compound **2** was determined by $^{19}F$ NMR chemical shifts in reference to [34].

#### 3.2.2. 2,3,3,3-Tetrafluoropropiophenone (3)

To the reaction mixture of **2** (3.7 g, 13.4 mmol) was added 3 M HCl at room temperature and then the mixture was stirred for 5 h. The reaction mixture was poured into 5% $NaHCO_3$ aq. and the organic products were extracted with $Et_2O$. The organic layer was washed with brine, and dried over $MgSO_4$. After removal of the solvent, distillation (0.5 mmHg, 50 °C) provided a pale yellow solid of **3** (2.6 g, 97% yield based on compound **1**); mp = 35–36 °C; IR (neat): 1700, 1600, 1452, 1334, 1148, 860 $cm^{-1}$; $^{1}H$ NMR (600 MHz, $CDCl_3$) $\delta$ 5.73 (1H, dq, $J$ = 46.8, 6.6 Hz, CHF), 7.52–7.55 (2H, m), 7.67–7.69 (1H, m), 8.00 (2H, d, $J$ = 8.4 Hz); $^{13}C$ NMR (150 MHz, $CDCl_3$): $\delta$ 87.7 (dq, $J$ = 199, 33 Hz, CHF), 120.7 (dq, $J$ = 26, 281 Hz, $CF_3$), 128.9, 129.3, 129.4, 133.6, 134.9, 188.0 (d, $J$ = 20 Hz, C=O); $^{19}F$ NMR (564 MHz, $CDCl_3$): $\delta$ −38.9 (1F, dq, $J$ = 47, 12 Hz), 87.4 (3F, dd, $J$ = 7, 12 Hz, $CF_3$); EI MS *m*/*z* (relative intensity): 206 $[M]^+$ (3), 105 $[M–CHFCF_3]^+$ (100), 77 $[Ph]^+$ (89).




Scheme 3.

#### 3.2.3. 1-Phenyl-3,3,3-trifluoro-1-trimethylsiloxypropene (4)

A suspension of $Me_3Si$–Cl (5 mL, 40 mmol) in distilled THF (30 mL) and Mg (turnings) (0.49 g, 20 mmol) was cooled to 0 °C under argon atmosphere. A solution of compound **3** (2.06 g, 10 mmol) in distilled THF (10 mL) was added dropwise and then the mixture was stirred for 1 h. After

evaporation of most of THF, *n*-hexane was added to the residue, and the resulting salt was filtered. Evaporation of filtrate and distillation (0.2 mmHg, 50 °C) provided a colorless oil of **4** (2.34 g, 90%) as a mixture of *E*/*Z* isomers (5:95 by $^{19}$F NMR). IR (neat): 2972, 1654, 1366, 1190, 1110 cm$^{-1}$; $^{1}$H NMR (600 MHz, $CDCl_3$): (*E* isomer) $\delta$ 0.19 (9H, s, $Me_3Si$), 5.20 (1H, q, $J$ = 8.4 Hz), 7.36–7.42 (3H, m), 7.49–7.51 (2H, m), (*Z* isomer) $\delta$ 0.15 (9H, s, $Me_3Si$), 5.35 (1H, q, $J$ = 7.8 Hz), 7.36–7.42 (3H, m), 7.49–7.51 (2H, m); $^{13}$C NMR (150 MHz, $CDCl_3$): (*E* isomer) $\delta$ 0.28 ($Me_3Si$), 99.2 (q, $J$ = 33 Hz), 123.7 (q, $J$ = 267 Hz, $CF_3$), 126.7, 128.4, 130.0, 136.9, 159.6 (q, $J$ = 6 Hz), (*Z* isomer) $\delta$ 0.09 ($Me_3Si$), 99.8 (q, $J$ = 35 Hz), 161.1 (q, $J$ = 6 Hz); $^{19}$F NMR (564 MHz, $CDCl_3$): (*E* isomer) $\delta$ 108.5 (3F, d, $J$ = 8 Hz), (*Z* isomer) $\delta$ 104.9 (3F, d, $J$ = 8 Hz); EI MS *m*/*z* (relative intensity): 260 $[M]^+$ (15), 245 $[M–Me]^+$ (5), 181 $[M - 79]^+$ (15), 149 $[M - 111]^+$ (17), 105 $[M - 155]^+$ (36), 77 $[Ph]^+$ (100), 73 $[Me_3Si]^+$ (31).

The stereochemistry of the compound **4** was determined by $^{1}$H and $^{19}$F NMR chemical shifts in reference to [21]. Ref. [21] reports that the synthesis of **4** by *O*-silylation of the 3,3,3-trifluoropropiophenone with $Me_3SiOTf$ gives only *Z* isomer.

### 3.2.4. 3,3,3-Trifluoro-1-phenyl-1,2-propanedione, hydrate (7)

To a solution of *m*-CPBA (2.6 g, 15 mmol) in distilled $CH_2Cl_2$ (20 mL) was added **2** (1.4 g, 5 mmol) at room temperature under an argon atmosphere. The reaction mixture was stirred for 2.5 h. The precipitated *m*-chlorobenzoic acid was removed by filtration. The organic layer was washed with $NaHCO_3$ solution and brine, and then dried over $MgSO_4$. After removal of the solvent, distillation (0.5 mmHg, 50 °C) provided a yellow liquid of **6** (Yield by $^{19}$F NMR: 86%, GC purity: 88%). Crude **6** was used for the next desilylative-defluorination reaction.

Compound **6** was added to a mixture of TBAT (13 mg, 0.025 mmol) in distilled $CH_2Cl_2$ (10 mL), and then the resulting mixture was stirred for additional 10 min at room temperature. After removal of the solvent from the crude reaction mixture, recrystallization (*n*-hexane/$Et_2O$) afforded **7** in 72% yield based on compound **2** as a pale yellow powder.

*3.2.4.1. 2,3,3,3-Tetrafluoro-2-trimethylsiloxypropiophenone (6).* IR (neat): 2972, 1706, 1602, 1452, 1216, 862 cm$^{-1}$; $^{1}$H NMR (600 MHz, $CDCl_3$): $\delta$ 0.23 (9H, s, $Me_3Si$), 7.48–7.50 (2H, m), 7.62–7.7.65 (1H, m), 8.12 (2H, d, $J$ = 7.2 Hz); $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ 0.73 ($Me_3Si$), 104.8 (dq, $J$ = 238, 35 Hz), 119.9 (dq, $J$ = 37, 287 Hz, $CF_3$), 120.7, 128.5, 130.4, 132.6, 134.3, 188.8 (d, $J$ = 29 Hz, C=O); $^{19}$F NMR (564 MHz, $CDCl_3$): $\delta$ 49.5 (1F, s), 80.6 (3F, d, $J$ = 3 Hz, $CF_3$); EI MS *m*/*z* (relative intensity): 193 $[M - 101]^+$ (1), 105 $[C(=O)Ph]^+$ (100), 77 $[Ph]^+$ (84).

*3.2.4.2. 3,3,3-Trifluoro-1-phenyl-1,2-propanedione, hydrate (7).* mp = 82–84 °C; IR (neat): 3424 (br), 1682, 1602, 1254, 1194, 1086 cm$^{-1}$; $^{1}$H NMR (600 MHz, $CDCl_3$): $\delta$ 4.97 (2H, s, OH), 7.49–.52 (2H, m), 7.66–7.69 (1H, m), 8.33 (2H, d, $J$ = 7.8 Hz); $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ 93.9 (q, $J$ = 34 Hz), 121.5 (q, $J$ = 286 Hz, $CF_3$), 128.5, 128.7, 129.3, 130.2, 131.8, 135.2, 191.8; $^{19}$F NMR (564 MHz, $CDCl_3$): $\delta$ 80.5 (3F, s); EI MS *m*/*z* (relative intensity): 105 (100), 77 (98).

The spectral data were consistent with those reported [35].

### 3.2.5. 2-Chloro-2,3,3,3-tetrafluoropropiophenone (8a)

To a solution of NCS (400 mg, 3.03 mmol) in DMF (6 ml) was added **2** (830 mg, 3.00 mmol) at room temperature under an argon atmosphere. The reaction mixture was stirred for additional 1 h. After removal of the solvent, purification of crude product by chromatography on silica gel (*n*-hexane, Rf = 0.60) afforded **8a** (700 mg, 97%) as a colorless oil. IR (neat): 3076, 1712, 1600, 1452, 1298, 1220, 690 cm$^{-1}$; $^{1}$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.52–7.55 (2H, m), 7.68–7.71 (1H, m), 8.12–8.14 (2H, m); $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ 100.5 (dq, $J$ = 270, 35 Hz), 119.7 (dq, $J$ = 30, 284 Hz, $CF_3$), 128.8, 128.9, 130.3, 130.4, 130.6–130.7 (m), 135.1, 183.9 (d, $J$ = 26 Hz); $^{19}$F NMR (564 MHz, $CDCl_3$): $\delta$ 31.1 (1F, q, $J$ = 6 Hz), 83.5 (3F, d, $J$ = 6 Hz, $CF_3$); EI MS *m*/*z* (relative intensity): 135 $[M–C(=O)Ph]^+$ (1), 127 $[M - 133]^+$ (4), 105 $[C(=O)Ph]^+$ (100), 77 $[Ph]^+$ (92); Anal. Calcd for $C_9H_5ClF_4O$: C, 44.27; H, 2.09. Found: C, 44.17; H, 2.05.

### 3.2.6. 2-Bromo-2,3,3,3-tetrafluoropropiophenone (8b)

To a solution of NBS (550 mg, 3.03 mmol) in DMF (6 mL) was added **2** (830 mg, 3.00 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred for additional 1 h. After removal of the solvent, purification of crude product by chromatography on silica gel (*n*-hexane, Rf = 0.30) afforded **8b** (850 mg, 99%) as a colorless oil. IR (neat): 3076, 1704, 1600, 1494, 1296, 1222, 1190, 898, 838 cm$^{-1}$; $^{1}$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.52–7.55 (2H, m), 7.67–7.70 (1H, m), 8.14–8.16 (2H, m); $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ 93.9 (dq, $J$ = 279, 34 Hz), 119.9 (dq, $J$ = 30, 283 Hz, $CF_3$), 128.8, 128.9, 130.3, 130.4, 130.8–130.9 (m), 135.0, 184.6 (d, $J$ = 25 Hz, C=O); $^{19}$F NMR (564 MHz, $CDCl_3$): $\delta$ 27.1 (1F, q, $J$ = 8 Hz), 85.4 (3F, d, $J$ = 8 Hz, $CF_3$); EI MS *m*/*z* (relative intensity): 127 $[M - 157]^+$ (6), 105 $[C(=O)Ph]^+$ (100), 77 $[Ph]^+$ (63); Anal. Calcd for $C_9H_5BrF_4O$: C, 37.92; H, 1.77. Found: C, 37.78; H, 1.61.

### 3.2.7. 2-Phenylthio-2,3,3,3-tetrafluoropropiophenone (8c)

To a solution of NCS (440 mg, 3.30 mmol) in distilled $CH_2Cl_2$ (12 mL) was added PhSH (360 mg, 3.30 mmol) at 0 °C. After stirring at 0 °C for 1 h, to the yellow suspension was added a solution of **2** (830 mg, 3.00 mmol) in distilled DMF (6 mL) at room temperature under an argon atmosphere. The reaction mixture was stirred for additional 1 h. The reaction was quenched by the addition of water (10 mL). The aqueous layer was extracted with *n*-hexane and the organic layer was dried over $MgSO_4$. After removal of the solvent, purification of crude product by chromatography on silica gel (*n*-hexane, Rf = 0.55) afforded **8c** (850 mg, 91%) as a colorless oil. IR (neat): 3076, 1698, 1600, 1446, 1208, 1188, 838, 690 cm$^{-1}$; $^{1}$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.29–7.33 (2H, m), 7.38–7.42 (3H, m), 7.55–7.58 (1H, m), 7.60–7.61 (2H, m), 7.86–7.88 (2H, m); $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ 103.9 (dq, $J$ = 246, 31 Hz), 121.3

(dq, $J$ = 33, 285Hz, $CF_3$), 124.8, 128.2, 128.3, 129.3, 129.8, 129.9, 130.8, 133.9, 137.3, 189.2 (d, $J$ = 26 Hz, C=O); $^{19}F$ NMR (564 MHz, $CDCl_3$): $\delta$ 18.0 (1F, q, $J$ = 11 Hz), 89.0 (3F, d, $J$ = 11 Hz, $CF_3$); EI MS $m/z$ (relative intensity): 314 $[M]^+$ (0.4), 105 $[C(=O)Ph]^+$ (100), 77 $[Ph]^+$ (34); Anal. Calcd for $C_{15}H_{10}F_4OS$: C, 57.32; H, 3.21. Found: C, 57.07; H, 3.18.

### 3.2.8. 2-Methoxyphenylmethyl-2,3,3,3-tetrafluoropropiophenone (**8d**)

To a mixture of **2** (280 mg, 1.00 mmol) and benzaldehyde dimethyl acetal (156 mg, 1.00 mmol) in distilled $CH_2Cl_2$ (2 mL) which was cooled to 0 °C under an argon atmosphere was added $Me_3SiOTf$ (220 mg, 1.00 mmol). The resulting mixture was stirred for an additional 4 h and then was poured into 5% $NaHCO_3$ aq. The organic products were extracted with $Et_2O$. The organic layer was washed with brine, and dried over $MgSO_4$. After removal of the solvent, purification of crude product by chromatography on silica gel (*n*-hexane:$Et_2O$ = 5: 1, Rf = 0.50) afforded **8d** (300 mg, 95%) as a colorless oil. Diastereomer mixture (65:35 by $^1H$ NMR); IR (neat): 3072, 2944, 1696, 1602, 1450, 1208, 1098 $cm^{-1}$; $^1H$ NMR (600 MHz, $CDCl_3$): major $\delta$ 3.17 (3H, s, OMe), 5.02 (1H, d, $J$ = 26.4 Hz), minor $\delta$3.34 (3H, s, OMe), 5.09 (1H, d, $J$ = 25.8 Hz); $^{13}C$ NMR (150 MHz, $CDCl_3$): major $\delta$ 57.3, 82.7 (dd, $J$ = 17, 1 Hz), 99.9 (dq, $J$ = 216, 28 Hz), 120.8 (dq, $J$ = 28, 285 Hz, $CF_3$), minor $\delta$ 57.4, 89.9 (d, $J$ = 11 Hz, 3F), 82.4 (dd, $J$ = 17, 1 Hz), 100.1 (dq, $J$ = 214, 29 Hz), 121.6 (dq, $J$ = 30, 286 Hz, $CF_3$); $^{19}F$ NMR (564 MHz, $CDCl_3$): major $\delta$ −24.2 (1F, m), 89.3 (3F, d, $J$ = 7 Hz, $CF_3$), minor $\delta$ −24.5 (1F, m), 89.9 (3F, d, $J$ = 11 Hz, $CF_3$); EI MS $m/z$ (relative intensity): 307 $[M-19]^+$ (1), 190 $[M-136]^+$ (6), 121 $[CH(OMe)Ph]^+$ (100), 105 $[C(=O)Ph]^+$ (86), 77 $[Ph]^+$ (39); Anal. Calcd for $C_{17}H_{14}F_4O_2$: C, 62.58; H, 4.32. Found: C, 62.58; H, 4.31.

### 3.2.9. 2-Bromo-3,3,3-trifluoropropiophenone (**9a**)

To a solution of NBS (195 mg, 1.10 mmol) in DMF (4 mL) was added **4** (260 mg, 1.00 mmol) at 60 °C under argon atmosphere. The reaction mixture was stirred for additional 1 h. After removal of the solvent, purification of crude product by chromatography on silica gel (*n*-hexane, Rf = 0.30) afforded **9a** (850 mg, 97%) as a colorless solid.; mp = 42–43 °C; IR (neat): 3004, 1694, 1372, 1268, 1150, 1112 $cm^{-1}$; $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 5.45 (1H, q, $J$ = 6.6 Hz), 7.53–7.56 (2H, m), 7.66–7.69 (1H, m), 7.97–7.99 (2H, m); $^{13}C$ NMR (150 MHz, $CDCl_3$): $\delta$ 39.9 (q, $J$ = 32 Hz), 122.4 (q, $J$ = 277 Hz, $CF_3$), 128.9, 129.1, 133.3, 134.7, 186.4 (C=O); $^{19}F$ NMR (564 MHz, $CDCl_3$): $\delta$ 94.1 (3F, d, $J$ = 6 Hz); EI MS $m/z$ (relative intensity): 105 $[C(=O)Ph]^+$ (100), 77 $[Ph]^+$ (72); Anal. Calcd for $C_9H_6BrF_3O$: C, 40.48; H, 2.26. Found: C, 40.49; H, 2.11.

### 3.2.10. 2,2-Dichloro-3,3,3-trifluoropropiophenone (**10b**)

To a solution of NCS (420 mg, 3.15 mmol) in DMF (4 mL) was added **4** (390 mg, 1.50 mmol) at 60 °C under an argon atmosphere. The reaction mixture was stirred at 60 °C for 1 h. After removal of the solvent, purification of crude product by chromatography on silica gel (*n*-hexane, Rf = 0.60) afforded **10b** (370 mg, 96%) as a colorless oil. IR (neat): 3068, 1712, 1600, 1452, 1258, 1196, 864 $cm^{-1}$; $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 7.51 (2H, t, $J$ = 8.4 Hz), 7.64–7.67 (1H, m), 8.26–8.28 (2H, m); $^{13}C$ NMR (150 MHz, $CDCl_3$): $\delta$ 78.4 (q, $J$ = 31 Hz), 121.2 (q, $J$ = 282 Hz, $CF_3$), 128.5, 130.2 (q, $J$ = 2 Hz), 130.8, 134.5, 182.5 (d, $J$ = 1 Hz, C=O); $^{19}F$ NMR (564 MHz, $CDCl_3$): $\delta$ 86.8 (3F, s); EI MS $m/z$ (relative intensity): 105 $[C(=O)Ph]^+$ (100), 77 $[Ph]^+$ (72); Anal. Calcd for $C_9H_5Cl_2F_3O$: C, 42.05; H, 1.96. Found: C, 42.04; H, 1.93.

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