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A Preparation of Trifluorolactic Aldehyde

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Abstract: A five-step preparation of 2-benzoyloxy-3,3,3-trifluoropropanal from 1,2-epoxy-3,3,3-trifluoropropane via Pummerer rearrangement is described. The total yield of the aldehyde from the epoxide was 90%. The aldehyde kept its optical purity when it was in hydrate form, but it was found to readily racemize in its formyl form. The utilization of selenium instead of sulfur in these procedures offered advantages in controlled oxidation of the heteroatom for Pummerer rearrangement and the subsequent hydrolysis of Pummerer product, an aldehyde equivalent.

Introduction

The titled compound, trifluorolactic aldehyde has been a target in the field of organofluorine chemistry, because it has potential applicability as a promising building block for further synthesis of fluorinated organic compounds, especially trifluoromethylated sugars.[1] An appearance of this aldehyde had been once traced by Resnati's group with using Pummerer rearrangement of the sulfoxide,[2] however their report showed only an ^{1}H NMR evidence and lacked in detailed properties of the compound. They used their compound only for synthesis of the optically active 3,3,3-trifluorolactic acid, in spite of its potentially wide applicability as an aldehyde itself.

Similar to the Resnati's method, some trifluorolactic aldehyde equivalents have been synthesized by means of oxidative processes using sulfur as an anchor for oxidation, such as an electrolytic acylation,[3] an electrolytic alkoxylation,[4] and a chlorination with sulfuryl chloride.[5] These processes gave the aldehyde equivalents in moderate to good yields (40 - 70%). However, hydrolyses of these equivalents to the target aldehyde have been unsuccessful and resulted in recovery of the equivalent and/or production of complex mixtures of sulfur containing compounds.[6]

Here, we applied a selenium analogue instead of sulfur to make the hydrolysis much easier, of which transformation resulted in higher yield of oxidation process as well as successful hydrolysis of the Pummerer product to trifluorolactic aldehyde. A characteristic feature of the trifluorolactic aldehyde and its reactivities are also reported herein.

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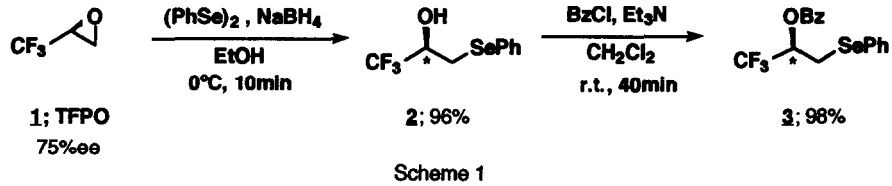
Results and Discussion

Synthesis of trifluorolactic aldehyde

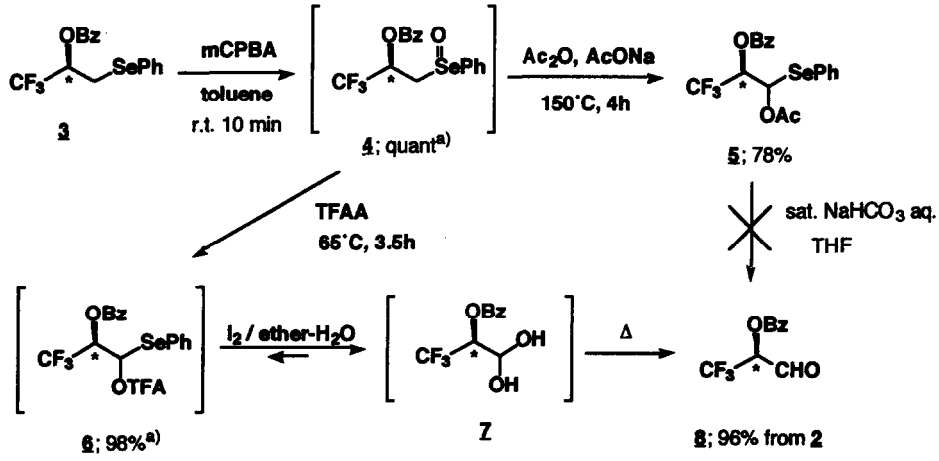
The starting material, 2-benzoyloxy-3,3,3-trifluoro-1-phenylselenopropane (**3**) was prepared by ring-opening reaction of commercially available optically active (*S*: 75% ee) 3,3,3-trifluoropropene oxide (**1**) with benzeneselenolate anion generated from diphenyl diselenide with $NaBH_4$, followed by protection of its hydroxyl group (Scheme 1).



Scheme 1

Both ring opening and protection underwent very smoothly and gave products **2** and **3** in excellent yields, 96% and 98%, respectively.

Oxidation of the selenide **3** with *m*-chloroperbenzoic acid gave selenoxide **4** quantitatively.[7] The selenoxide was rather unstable so that the Pummerer rearrangement was successively conducted in the same pot. The Pummerer rearrangement with acetic anhydride gave 1-acetoxy-2-benzoyloxy-3,3,3-trifluoro-1-phenylselenopropane (**5**) in 75% isolated yield from selenide **3**. Although O,Se-acetal **5** was stable enough to be isolated, it was not hydrolyzed by saturated sodium bicarbonate. Pummerer rearrangement promoted by trifluoroacetic anhydride (TFAA) gave 2-benzoyloxy-3,3,3-trifluoro-1-trifluoroacetoxy-1-phenylselenopropane (**6**) in 98% yield, almost quantitatively.[7] The compound **6** was found to be sensitive to moisture and was partially converted to the hydrated form of trifluorolactic aldehyde (**7**), to formyl form, as well as to its polymer-



Scheme 2

ic form, during its isolation by silica gel chromatography.

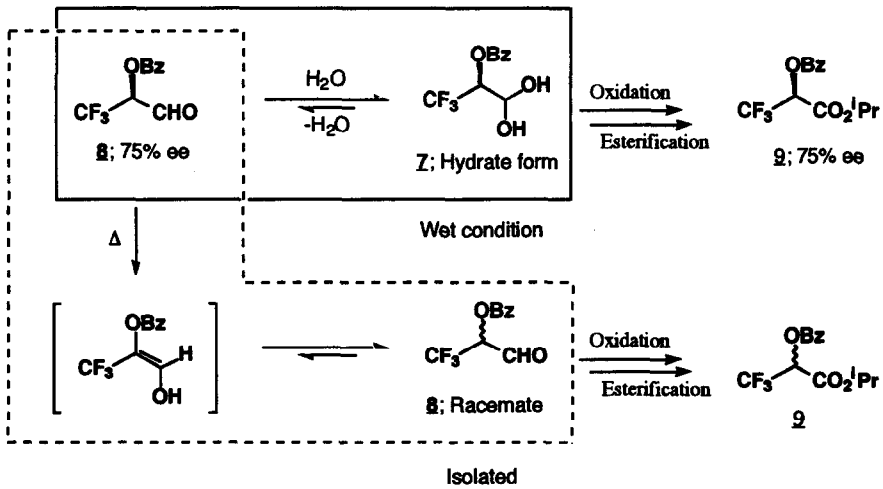
Without further purification, the Pummerer reaction mixture containing the compound **6** was dissolved in diethyl ether, and then hydrolyzed by I_2/H_2O-ether biphase system. This hydrolysis converted the compound **6** to the hydrate of aldehyde **7** and diphenyl diselenide smoothly.

Kugelrohr distillation (90 °C/14 mmHg) of this hydrate **7** gave aldehyde **8** (>96% in chemical purity) in 96% isolated yield via four steps from selenide **3** (Scheme 2). Interestingly, a high vacuum distillation with ambient temperature (40 °C /10^{-4} mmHg) gave no appreciable amount of the aldehyde and resulted in recovery of hydrate **7** as a residue. This result suggests the dehydration needs heating of compound **7**.

Nature of trifluorolactic aldehyde and its hydrate form

2-Benzoyloxy-3,3,3-trifluoropropanal (**8**) was a colorless liquid, with the following spectroscopic properties: The formyl form of the compound was confirmed by ^{1}H NMR (9.7 ppm, q, $^4J_{HF}$ = 2 Hz, 1H), ^{13}C NMR (188.6 ppm), and IR (1740 cm^{-1}). When the isolated aldehyde **8** was dissolved in acetone-d_6 with a small amount of D_2O, the typical formyl peak of ^{1}H NMR spectra (d, 9.7 ppm) disappeared within one minute and there appeared a few new peaks attributable to the hydrate **7**. ^{19}F NMR (acetone-d_6, D_2O, 188 MHz, C_6F_6 as a chemical shift standard): 90.8 (d, $^3J_{FH}$ = 6 Hz) ppm; ^{1}H NMR (acetone-d_6, D_2O, 200 MHz): 5.3 (d, $^3J_{HH}$ = 6 Hz, 1H), 5.5 (dq, $^3J_{HF}$ = 6 Hz, $^3J_{HH}$ = 6 Hz, 1H), 7.5-7.7 (m, 3H), 8.0-8.1 (m, 2H) ppm.

To ascertain the optical purity of the trifluorolactic aldehyde and its hydrate, they were oxidized and esterified to 2-propyl trifluorolactate (**9**) respectively,[2] which was then compared with the authentic trifluorolactate.[8] Optical purity of the hydrate **7** with certain amount of water[9] was retained to be 75% ee,[10] which was same as that of the starting epoxide. Meanwhile, the aldehyde isolated by distillation was found to racemize to 11% ee[10] even soon after the distillation.



Scheme 3

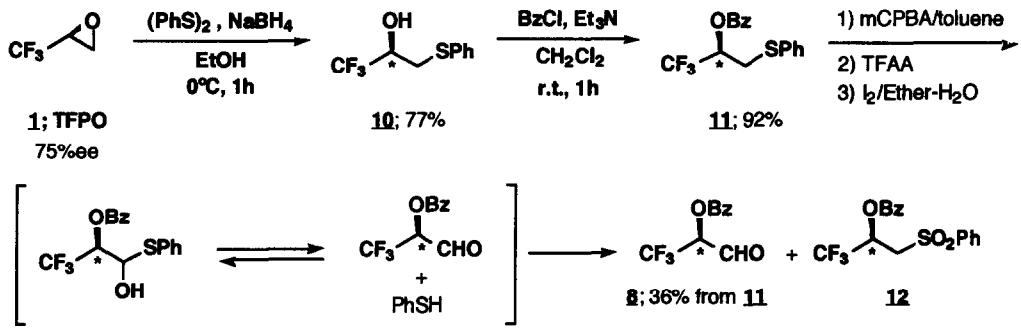
When the aldehyde was co-distilled with water, we found aldehyde hydrate was also readily racemized,

and the optical purity of the trapped hydrate was 23% ee.[10] These results suggested that the aldehyde lost its optical purity when it was isolated as an aldehyde form, while it retains its optical purity under a wet condition (Scheme 3).[2]

Advantage of selenium in the trifluorolactic aldehyde synthesis

When we traced the trifluorolactic aldehyde synthesis by the same strategy with the sulfur synthon (**11**), some advantages of selenium in the aldehyde synthesis were clarified. The first one was controlled oxidation of selenium moiety for preparation of selenoxide, the second was an efficient Pummerer rearrangement, and the third was efficient elimination of selenolate anion generated in the course of hydrolysis of the aldehyde equivalent.

The starting material, 2-benzoyloxy-3,3,3-trifluoro-1-phenylthiopropane **11** was prepared by the same procedure as that of selenide (Scheme 4). Both ring opening and protection underwent very smoothly and gave products **10** and **11** in good yields, 77% and 92%, respectively. Oxidation of the sulfide **11** with *m*-chloroperbenzoic acid followed by Pummerer rearrangement and hydrolysis resulted in production of 36% isolated yield of trifluorolactic aldehyde via four steps from sulfide **11** (Scheme 4). The major by-product was sulfone **12**, an over oxidation product of sulfide **11**.



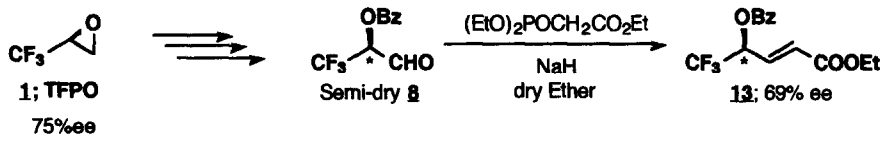
Scheme 4

Total consumption of I_2 in the hydrolysis was estimated by visible absorption of remained I_2 in the solution. Hydrolysis of O,Se-acetal consumed 0.72 eq. amount of I_2 and O,S-acetal consumed 0.24 eq. amount. This result suggested a more effective oxidative elimination of benzeneselenenyl moiety from reacting solution as diphenyl diselenide, of which formation promoted favorable shift of the possible equilibrium between O,Se-hemiacetal and aldehyde (Scheme 2).

Synthetic utilization of trifluorolactic aldehyde and its hydrate

The trifluorolactic aldehyde was used for Wittig - Horner reaction to produce α,β–unsaturated ester **13**. Semi-dried ether layer of hydrolysis reaction mixture was subjected to the Wittig-Horner reaction. The reaction gave α,β–unsaturated ester **13** in 47% yield (Scheme 5). The product was purified and analyzed by chiral HPLC. The optical purity of the Wittig – Horner product **13** was found to be 69% ee, suggesting 6% ee loss of optical purity from epoxide **1**. This change in optical purity suggested 6% of the aldehyde **8** was racemized

under the present Wittig – Horner procedure.



Scheme 5

In conclusion, we succeeded in preparation and isolation of trifluorolactic aldehyde in excellent yields. Though the aldehyde was found to racemize readily when it was dried and isolated, it retained its optical purity so long as the compound was kept under a wet condition. The synthetic applications of the aldehyde are now in progress.

Acknowledgment.

We thank SC-NMR Laboratory of Okayama University for ^{19}F NMR analyses. The financial supports by Okayama Foundation for Science and Technology and the Ministry of Education, Science, Culture and Sports (No. 09305058) are also gratefully acknowledged.

Experimental Section

General Procedure. IR spectra were measured on Hitachi Model 270-30 Infrared Spectrometer. ^1H (200 MHz), ^{19}F (188 MHz), and ^{13}C (50.3 MHz) NMR spectra were recorded by Varian VXR apparatus and the chemical shifts are reported in δ ppm values relative to TMS (δ 0.0 ppm for ^1H and ^{13}C NMR) and C_6F_6 (δ 0.0 ppm for ^{19}F NMR). For the quantitative analysis of yields, 1,3-bis(trifluoromethyl)benzene was used as an internal standard for ^{19}F NMR. Coupling constants (J) are reported in Hz. Optical rotation was measured in a cell with 50 mm length and 1 mL capacity using a Horiba High Sensitive Polarimeter SEPA-300. Elemental analyses were performed on Perkin Elmer series II CHNS/O Analyzer 2400. GC/MS were performed on a Hewlett-Packard HP5971A. All commercially available reagents and solvents were employed without further purification. E. Merck silica gel (Kieselgel 60, 230-400 mesh) was employed for the chromatography. R_f values for all compounds described were taken on TLC plates (E. Merck, Kieselgel 60 F254), using hexane/diethyl ether (5:1) as an eluent. Enantiomeric excesses of 2-propyl 2-benzoyloxy-3,3,3-trifluoropropanoate from trifluorolactic acid[8] and that compound derived from present aldehyde, ethyl 4-benzoyloxy-5,5,5-trifluoro-2-pentenoate were determined by HPLC analysis equipped with chiral column (Daicel Chiralcel OJ with an eluent of hexane/2-propanol).

(*S*)-3,3,3-Trifluoro-1-phenylseleno-2-propanol (2). A mixture of diphenyl diselenide (1.61 g, 5.12 mmol) and $NaBH_4$ (0.428 g, 11.32 mmol) was dissolved in dry ethanol (20 mL) under a nitrogen atmosphere at 0 °C. After 20 min stirring, 75% ee (*S*)-3,3,3-trifluoropropene oxide (**1**: 2.64 g, 23.5 mmol) was added to the stirred solution at 0 °C. The reaction mixture was stirred for 15 min, and quenched by adding 2 mL of saturated NH_4Cl aq. The aqueous layer was extracted with ether (2 mL × 3), and the combined organic phase was washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (Hexane : Ether (20 : 1) elute) to give slightly yellowish oil **2** (2.66 g, 9.87 mmol, 96%): R_f = 0.32; $[\alpha]^{18}_D$ = -41.7 (*c* 6.42 in $CHCl_3$); ^1H NMR 3.0 (dd, 1H,

$^3J_{HH}$ = 10 Hz, $^2J_{HH}$ = 13 Hz), 3.2 (dd, 1H, $^3J_{HH}$ = 3 Hz, $^2J_{HH}$ = 13 Hz), 3.3 (s, 1H), 3.9-4.1 (m, 1H), 7.3 (m, 3H), 7.5-7.6 (m, 2H); ^{13}C NMR 28.0, 69.0 (q, $^2J_{CF}$ = 31 Hz), 124.1 (q, $^1J_{CF}$ = 282 Hz), 127.8, 129.3, 133.2; ^{19}F NMR 82.8 (d, $^3J_{FH}$ = 6 Hz); GC/MS m/z 270 (M^+, 47), 268 (22), 171 (54), 169 (26), 158 (21), 157 (35), 155 (20), 93 (29), 91 (100), 78 (31), 77 (48), 69(6), 51 (43), 50 (18); IR(neat) 3472 cm^{-1}; Element. Anal. Found: C, 40.05; H, 3.64 (Calc. for $C_9H_9F_3OSe$: C, 40.17; H, 3.37).

(*S*)-2-Benzoyloxy-3,3,3-trifluoro-1-phenylselenopropane (3). Triethylamine (286 mg, 2.83 mmol) and benzoyl chloride (0.232 g 1.65 mmol) were added to a solution of **2** (261 mg, 0.970 mmol) in CH_2Cl_2 (3 mL) under a nitrogen atmosphere at 0 °C. Then the solution was warmed up to room temperature. After being stirred for 60 min, the reacting solution was quenched by 10% HCl (2 mL). The aqueous layer was extracted with ether (2 mL × 3), and the combined organic layer was washed by saturated $NaHCO_3$ aq., dried over $MgSO_4$, and concentrated to dryness. Purification of the residue by column chromatography (Hexane : Ether (20 : 1)) gave slightly yellowish oily product **3** (0.355 g, 0.950 mmol, 98%): R_f = 0.58; $[\alpha]^{18}_D$ = -96.0 (*c* 4.02 in $CHCl_3$); ^{1}H NMR 3.2 (dd, 1H, $^3J_{HH}$ = 9 Hz, $^2J_{HH}$ = 14 Hz), 3.3 (dd, 1H, $^3J_{HH}$ = 5 Hz, $^2J_{HH}$ = 14 Hz), 5.7 (m, 1H), 7.2-7.3 (m, 3H), 7.4-7.7 (m, 5H), 8.0 (m, 2H); ^{13}C NMR 25.0, 69.5 (q, $^2J_{CF}$ = 32 Hz), 132.2 (q, $^1J_{CF}$ = 282 Hz), 127.9, 128.1, 128.3, 129.2, 130.0, 133.6, 133.8, 164.5; ^{19}F NMR 85.1 (d $^3J_{FH}$ = 6 Hz); GC/MS m/z 374 (9), 252 (46), 250 (23), 249 (10), 217 (47), 183 (24), 181 (12), 157 (17), 105 (83), 91 (18), 78 (11), 77 (100), 60(1), 51 (34), 50 (10); IR(neat) 1738 cm^{-1}; Element. Anal. Found: C, 51.73; H, 3.37 (Calc. for $C_{16}H_{13}F_3O_2Se$: C, 51.49; H, 3.51).

1-Acetoxy-2-benzoyloxy-3,3,3-trifluoro-1-phenylselenopropane (5). A solution of *m*-CPBA (70.3 mg, 0.407 mmol) dissolved in toluene (1 mL) was added dropwise to the toluene solution (2 mL) of **3** (0.1134 g, 0.303 mmol) for oxidation of selenide to selenoxide. Quantitative conversion of selenide to selenoxide **4** was traced by ^{19}F NMR (diastereomer major: 85.4 (d, $^3J_{FH}$ = 6 Hz), minor: 85.5 (d, $^3J_{FH}$ = 6 Hz). After stirring 10 min, acetic anhydride (0.5 mL) and sodium acetate (28.4 mg, 0.346 mmol) was added to the reaction mixture. The solution was stirred for 4 h at 150 °C. And then cooled to the room temperature. Water was added to the solution and organic substances were extracted by ether (2 mL × 3). The solvent was removed under reduced pressure. Purification of the residue by column chromatography (Hexane : Ether (20 : 1) elute) gave oily product **5** (97.4 mg, 0.226 mmol, 75%, diastereomer): R_f = 0.42 and 0.34; ^{1}H NMR major: 2.1 (s, 3H), 5.8 (dq, $^3J_{HF}$ = 6 Hz, $^3J_{HH}$ = 7 Hz, 1H), 6.6 (d, $^3J_{HH}$ = 7 Hz, 1H), 7.3-7.4 (m, 3H), 7.4-7.7 (m, 5H), 8.0-8.1 (m, 2H); ^{19}F NMR 88.6 (m, mixture of diastereomer), minor: 2.1 (s, 3H), 5.9 (dq, $^3J_{HF}$ = 6 Hz, $^3J_{HH}$ = 3 Hz, 1H), 6.7 (d, $^3J_{HH}$ = 3 Hz, 1H), 7.3-7.4 (m, 3H), 7.4-7.7 (m, 5H), 8.0-8.1 (m, 2H); ^{19}F NMR 88.6 (m, mixture of two diastereomers); GC/MS m/z 432 (trace), 275 (18), 233 (8), 158 (14), 157 (17), 156 (9), 155 (11), 105 (47), 78 (10), 77 (46), 69(trace), 51 (12), 43 (100); IR(neat) 1748, 1760 cm^{-1}; Element. Anal. of a diastereomeric mixture Found: C, 50.42; H, 3.77 (Calc. for $C_{18}H_{15}F_3O_4Se$: C, 50.13; H, 3.51).

2-Benzoyloxy-3,3,3-trifluoropropanal (8). A solution of *m*-CPBA (120.6 mg, 0.699 mmol) dissolved in toluene (1 mL) was added dropwise to the toluene solution (0.5 mL) of **3** (182.2 g, 0.488 mmol), then the mixture was stirred for 10 min. Quantitative conversion of selenide to selenoxide **4** was traced by ^{19}F NMR (diastereomer major: 85.4 (d, $^3J_{FH}$ = 6 Hz), minor: 85.5 (d, $^3J_{FH}$ = 6 Hz). After adding TFAA (0.5 mL), the reaction mixture was stirred for 3.5 h at 65 °C. The solvent was removed under reduced pressure. 2-Benzoyloxy-3,3,3-trifluoro-1-trifluoroacetoxy-1-phenylselenopropane **6** was detected by ^{19}F NMR (diastereomer major: 88.5 (d, $^3J_{FH}$ = 6 Hz, CF_3CH-), minor: 88.8 (d, $^3J_{FH}$ = 6 Hz, CF_3CH-), 87.0 (s, CF_3CO_2)) in 98% yield (estimated by ^{19}F NMR analysis).

Water (2 mL), ether (1 mL) and iodine (188 mg, 0.742 mmol) were added to this reaction mixture. After stirring for 4 hours, saturated $Na_2S_2O_3$ aq. was added. The combined ether extracts were dried over $MgSO_4$. The solvent was removed in vacuo. The residue was purified by Kugelrohr distillation (90 °C / 14 mmHg) to get aldehyde **8** in 96% isolated yield, four steps from **3**. Enantiomeric excess of this ester was determined by chiral

HPLC with an eluent (Hexane:2-Propanol = 200:1): ^{1}H NMR 5.8 (q, 1H, $^3J_{HF}$ = 8 Hz), 7.5-7.7 (m, 3H), 8.1-8.2 (m, 2H), 9.7 (q, 1H, $^4J_{HF}$ = 2 Hz); ^{13}C NMR 74.5 (q, $^2J_{CF}$ = 31 Hz), 121.6 (q, $^1J_{CF}$ = 281 Hz), 127.4, 128.7, 130.3, 134.4, 164.3, 188.6; ^{19}F NMR 90.3 (d, $^3J_{FH}$ = 8 Hz); GC/MS m/z 232 (trace), 204 (7) 203 (4), 140 (2), 122 (10), 106 (12), 105 (100), 91 (8), 78 (7), 77 (81), 76 (7), 75 (4), 74 (6), 73 (1), 69 (6); IR(neat) 3492 (broad), 1740 (over lapped) cm^{-1}; Element. Anal. Found: C, 51.32; H, 3.29 (Calc. for $C_{10}H_7F_3O_3$: C, 51.74; H, 3.04).

2-Propyl 2-benzoyloxy-3,3,3-trifluoropropanoate (9). The authentic sample was prepared by esterification with 2-propanol and protection with benzoyl chloride of 75% ee trifluorolactic acid. The spectra of this compound gave good agreement with those of the compound derived from aldehyde (GC/MS, ^{1}H NMR, ^{19}F NMR) and have following spectroscopic characters: R_f = 0.34; ^{1}H NMR 1.3 (d, 3H, $^3J_{HH}$ = 6 Hz), 1.3 (d, 3H, $^3J_{HH}$ = 6 Hz), 5.2 (m, 1H), 5.6 (q, 1H, $^3J_{HF}$ = 7 Hz), 7.4-7.7 (m, 3H), 8.1 (m, 2H); ^{19}F NMR 89.1 (d, $^3J_{FH}$ = 7 Hz); GC/MS m/z 290 (trace), 204 (12) 105 (100), 91 (13), 77 (60), 51 (21), 50 (10), 91 (8), 69(3), 43 (79), 41 (18), 27 (10).

(*S*)-3,3,3-Trifluoro-1-phenylthio-2-propanol (10). A mixture of diphenyl disulfide (0.219 g, 1.00 mmol) and $NaBH_4$ (0.126 g, 3.33 mmol) was dissolved in ethanol (6 mL) under a nitrogen atmosphere at 0 °C. After 60 min stirring, 75% ee (*S*)-3,3,3-trifluoropropene oxide (**1**: 0.273 g, 2.43 mmol) was added to the stirred solution at 0 °C. The reaction mixture was stirred for 60 min, then quenched by adding 3 mL of sat. NH_4Cl aq. The aqueous layer was extracted with ether (3 mL × 3), and the combined organic phase was washed by saturated $NaHCO_3$, and brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (Hexane : Ether (25 : 1)) to give colorless oily product **10** (0.351 g, 1.58 mmol, 77%): R_f = 0.25(hexane : ether (5 : 1) ; ^{1}H NMR 3.0 (dd, 1H, $^3J_{HH}$ = 10 Hz, $^2J_{HH}$ = 13 Hz), 3.2 (dd, 1H, $^3J_{HH}$ = 3 Hz, $^2J_{HH}$ = 13 Hz), 3.3 (s, 1H), 3.9-4.1 (m, 1H), 7.2-7.5 (m, 5H); ^{13}C NMR 35.2, 68.4 (q, $^2J_{CF}$ = 31 Hz), 124.3 (q, $^1J_{CF}$ = 282 Hz), 127.5, 129.4, 130.7, 133.3; ^{19}F NMR 82.9 (d, $^3J_{FH}$ = 6 Hz); GC/MS m/z 222 (51), 135 (4), 123 (100), 109 (27), 91 (5), 78 (6), 77 (27), 69 (43), 51 (40), 45 (57); IR(neat) 3468 cm^{-1}; Element. Anal. Found: C, 48.30; H, 4.38; (Calc. for $C_9H_9F_3OS$: C, 48.64; H, 4.08).

(*S*)-2-Benzoyloxy-3,3,3-trifluoro-1-phenylthiopropane (11). Triethylamine (0.319 g, 3.16 mmol) and dry benzoyl chloride (0.218 g 1.55 mmol) were added to a solution of **10** (0.222 g, 1.00 mmol) in dry CH_2Cl_2 (3 mL) under a nitrogen atmosphere at 0 °C. Then the solution was warmed up to room temperature. After being stirred for 60 min, the reacting solution was quenched by 10% HCl (2 mL). The aqueous layer was extracted with ether (2 mL × 3), and the combined organic layer was washed by saturated $NaHCO_3$ aq. and brine. The mixture was dried over $MgSO_4$, and concentrated to dryness. Purification of the residue by column chromatography (Hexane : Ether (25 : 1)) gave colorless oily product **11** (0.302 g, 0.924 mmol, 92%): R_f = 0.53(hexane : ether (5 : 1)) ; ^{1}H NMR 3.2-3.4 (m, 2H), 5.7 (m, 1H), 7.2-7.3 (m, 3H), 7.4-7.7 (m, 5H), 8.0 (m, 2H); ^{13}C NMR 34.0, 69.6 (q, $^2J_{CF}$ = 32 Hz), 123.8 (q, $^1J_{CF}$ = 282 Hz), 128.1, 129.0, 129.8, 130.6, 132.0, 134.3, 134.3, 165.2; ^{19}F NMR 85.3 (d $^3J_{FH}$ = 6 Hz); GC/MS m/z 326 (5), 204 (36), 135 (40), 105 (40), 91 (5), 78 (8), 77 (100), 69 (13), 51 (58), 45 (31); IR(neat) 1744 cm^{-1}; Element. Anal. Found: C, 58.63; H, 4.35 (Calc. for $C_{16}H_{13}F_3O_2S$: C, 58.89; H, 4.02).

(*S*)-3,3,3-Trifluoro-2-benzoyloxypropylphenylsulfone (12). A solution of *m*-CPBA (0.378 g, 1.75 mmol) in dry CH_2Cl_2 (2 mL) was added dropwise to a solution of **11** (0.163 g, 0.499 mmol) in dry CH_2Cl_2 (2 mL) under an argon atmosphere at 0 °C. After being stirred for 3 h, the reacting solution was quenched by sat. $NaHCO_3$ aq. (3 mL). The aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was washed by brine. The mixture was dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (Hexane : Ether (3 : 2)) gave colorless needles **12** (m.p. 80°C, 0.177 g, 0.495 mmol, 99%): R_f = 0.38 (hexane : ether (4 : 3)) .; ^{1}H NMR 3.6 (dd, 2H, $^3J_{HH}$ =15 Hz, $^2J_{HH}$ =2 Hz), 3.8 (dd, 1H, $^3J_{HH}$ =15 Hz, $^2J_{HH}$ =10 Hz), 6.1 (ddq, 1H, $^3J_{HH}$ =10 Hz, $^3J_{HH}$ =2 Hz, $^3J_{FH}$ = 6 Hz), 7.3-7.9 (m,

10H); ^{19}F NMR 84.7 (d, $^{3}J_{FH}$ = 6 Hz); GC/MS m/z 358(3), 217(77), 141 (9), 122 (11), 105 (91), 77 (100), 69 (2), 51 (29); IR (neat) 1734, 1016 cm^{-1}; Element. Anal. Found: C, 53.86; H, 3.57 (Calc. for $C_{16}H_{13}F_3O_4S$: C, 53.63; H, 3.66).

Ethyl 4-benzoyloxy-5,5,5-trifluoro-2-pentenoate (13). Trifluorolactic aldehyde hydrate **7** was prepared in 0.5 mmol scale in situ. The reacting solution containing hydrate **7** was quenched by sat. $Na_2S_2O_3$ aq., then extracted by ethyl ether. The combined ether layer was washed with saturated $NaHCO_3$ aq, and dried over $MgSO_4$. The solvent was removed under vacuum. In an another flask, triethyl phosphonoacetate (0.13 mL, 0.65 mmol) was added to a solution of NaH (oil suspension 60%; 0.024 g, 0.6 mmol) in dry ethyl ether at room temperature under an argon atmosphere. After stirring for 1 h, the Wittig-Horner reagent was added dropwise through syringe to a cold solution of crude hydrate **7** dissolved in ethyl ether. After the mixture was stirred at -78 °C for 1 h, the mixture was allowed to warm to -20 °C over 2.5 h and then quenched with 1 mL of 10% HCl. The organic layer was separated, washed with brine, and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography on silica gel, eluting with a mixture of hexane-diethyl ether (20:1), to give the γ-benzoyloxy-α,β-unsaturated ester in 47% yield. Enantiomeric excess of this ester was determined by chiral HPLC with an eluent (Hexane:2-Propanol = 100:1).: R_f = 0.4; ^{1}H NMR 1.3 (t, 3H), 4.2 (q, 2H), 6.0-6.2 (m, 1H), 6.3 (dd, 1H), 7.0 (dd, 1H), 7.5-7.7 (m, 3H), 8.0 (m, 2H); ^{19}F NMR 86.1 (d, $^{3}J_{FH}$ = 6 Hz); Element. Anal. Found: C, 55.72; H, 4.49 (Calc. for $C_{14}H_{13}F_3O_4$: C, 55.63; H, 4.34).

Reference and Notes

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7) These yields were estimated by ^{19}F NMR.
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9) Although the hydrolysis reaction (0.5 mmol scale) in d_6-acetone-D_2O-I_2 (1 mmol) system gave no detectable peaks of **8** in the ^{19}F and ^{1}H NMR, distillation of the reaction mixture gave the aldehyde in 90% yield (0.45 mmol).
10) The optical purity was compared with 2-propyl 2-benzoyloxy-3,3,3-trifluoropropanoate derived from trifluorolactic acid (ref. 8).