Highly Stereocontrolled Access to 1,1,1-Trifluoro-2,3-epoxypropane via Lipase-Mediated Kinetic Resolution of 1,1,1-Trifluoro-3-(phenylthio)propan-2-ol and Its Application

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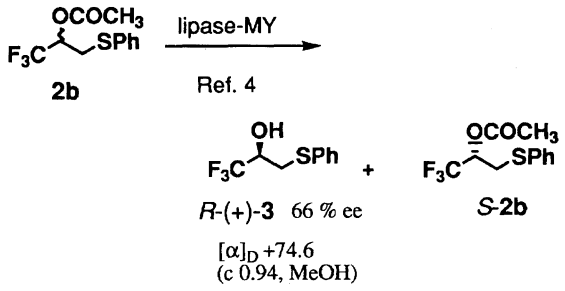
1,1,1-Trifluoro-3-(phenylthio)propan-2-ol was prepared in high enantiomeric purity by lipase-mediated kinetic resolution of the corresponding esters. The resolved alcohol was successfully converted into 1,1,1-trifluoro-2,3-epoxypropane and/or used in the subsequent reactions as latent 1,1,1-trifluoro-2,3-epoxypropane via sulfonium salt formation.

Ever increasing interest in the development of highly useful homochiral synthones has prompted us to investigate efficient methods. We previously reported the synthesis of 1-aryl-2,2,2-trifluoroethanol via bakers' yeast reduction of α,α,α-trifluoroacetophenone derivatives.[1] In this reduction, substrate specificity of the yeast-mediated process was overcome by introducing a substituent at the *para*-position of the aromatic ring, which also offers a good access for the construction of ferroelectric crystals. In an effort to develop new chiral synthones for the construction of useful homochiral materials involving ferroelectirc crystals, chiral 1,1,1-trifluoro-2,3-epoxypropane **4** appears to be an attractive building block.[2] Recently three procedures have been reported for the preparation of this compound, i. e., microbial oxidation of 3,3,3-trifluoroprop-1-ene,[3c] resolution of racemic trifluorolactic acid with chiral 2-amino-1-phenylpropane-1,3-diol followed by functional group manipulation,[3b] and enantioselective reduction of 1-bromo-3,3,3-trifluoropropan-2-one with *B*-chlorobis(isopinocampheyl)borane followed by ring-closure.[3a] However, some difficulties associated with the low boiling point of epoxide **4** call for due care on handling.[3] For use as a precursor of this particular epoxide **4**, 1,1,1-trifluoro-3-(phenylthio)propan-2-ol **3**[4] and its analogues seem to be candidates, due in part to their ready accessibility and handling, if they could be prepared in high enatiomeric purity. The facile transformation of the precursor **3** into **4** may offer another versatile approach to this useful class of compounds. Moreover, one-pot transformation of **3** into various useful trifluoromethyl alcohols via in situ formation of **4** also avoids otherwise tedious handling of the epoxide **4**.

Results and Discussion

Literature surveys[4,5] and our own examination into the reduction of ketone **1** have led us to the conclusion that the use of bakers' yeast reduction of the ketones **1** ($R^1 = CH_2SPh$, CH_2SO_2Ph, $CH(-SCH_2CH_2CH_2S-)$) containing sulfur functional groups met with only moderate success. Reduced alcohols were obtained in relatively low enantiomeric purity (51—67%ee) under a variety of reduction conditions involving those in the presence or absence of sucrose. Our previous studies have already disclosed the efficiency of the lipase-mediated kinetic resolution of fluorine-containing alcohols. In particular, lipase (Amano PS) was found to be suitable for the resolution of methoxyimino alcohols having fluorine substituents to give excellent precursors for the synthesis of fluorinated threonines.[6] With these findings in hand, we have examined the lipase mediated kinetic resolution of the ester **2** derived from 1,1,1-trifluoro-3-(phenylthio)propan-2-ol and subsequent transformations via formation of sulfonium salt.

Hitherto, lipase-mediated kinetic resolution of sulfur-containing trifluorinated alcohols, in particular, that of phenylthio derivative **2b** with lipase-MY, has been reported to give the hydrolized alcohol *R*-**3** in 66 %ee (vide infra).[4] In the present study, in order to obtain the desired epoxide **4** and its derivatives in high enantiomeric purity, the resolution of the precursor, ester **2**, under various conditions was examined.



(1)

Asymmetric Hydrolysis. The asymmetric hydrolysis of ester **2** was carried out with lipase (Amano PS) in acetone or THF and phosphate buffer at 35 °C for 2—79 h to give (*R*)-1,1,1-trifluoro-3-(phenylthio)propan-2-ol *R*-**3** and (*S*)-1,1,1-trifluoro-3-phenylthio-2-(acyloxy)propane *S*-**2**. The remaining ester *S*-**2** was hydrolyzed with K_2CO_3 in methanol–water at room temperature to give the corresponding alcohol *S*-**3** in quantitative yield without affecting the stereo-

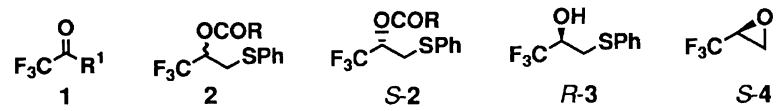
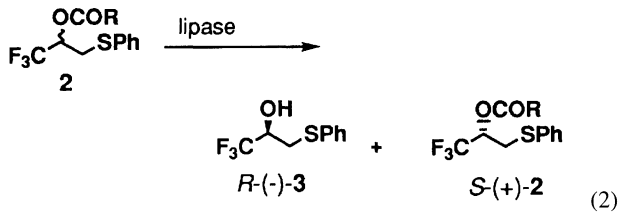


Chart 1.

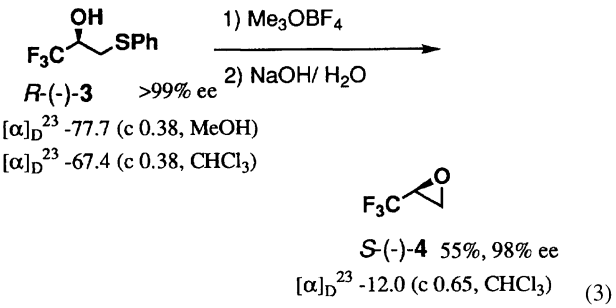
chemical integrity. The enantiomeric purity was determined by GLC analysis using a chiral stationary column (Chiraldex G-TA, 20 m) after transformation into the corresponding acetate with acetic anhydride–triethylamine in dichloromethane. Representative results are shown in Table 1.



(2)

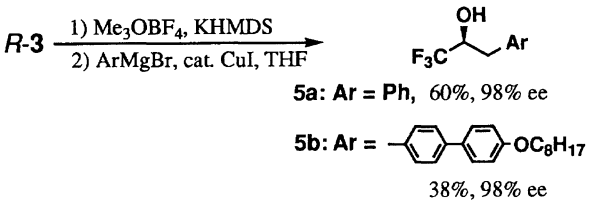
Although the hydrolysis of the formate **2a** proceeded at room temperature, the enantioselectivity was not sufficient, and both the alcohol and the ester were obtained in low enantiomeric excess (Entry 1). The hydrolysis did not proceed well at room temperature with the acetate **2b** and the propionate **2c**, and required 35 °C for completion. In the case of the acetate, THF appeared to be the solvent of choice, and the hydrolysis in THF gave alcohol *R*-**3** and acetate *S*-**2b** in good enantiomeric excess, whereas the use of acetone as solvent slightly decreased the enantioselectivity (Entries 2 and 3). The best result was obtained when the hydrolysis was conducted with the propionate in acetone, and both alcohol *R*-**3** and propionate *S*-**2c** were formed in excellent enantiomeric purity (Entries 4 and 5). As to the biocatalyst, the use of lipases (Sigma Type VII, from *Candida cylindracea*) and PPL was attempted besides lipase PS, but almost no enantio-discrimination was observed with these lipases. On the other hand, although enantioselective esterification by using vinyl acetate in the presence of lipases was also attempted, the reaction did not proceed with an appreciable rate under any of various conditions.

Transformation into Epoxide and Determination of the Absolute Configuration. The transformation of the hydrolyzed (−)-alcohol **3** into epoxide **4** was carried out via treatment with trimethyloxonium tetrafluoroborate, followed by 60% aq sodium hydroxide[7] to give 1,1,1-trifluoro-2,3-epoxypropane **4** in 55% yield. Comparison of the specific rotation of obtained **4** with that reported[3] established the configuration of hydrolyzed (−)-alcohol **3** to be *R*. This result was opposite to that previously reported,[4] which showed (+)-alcohol **3** had *R*-configuration. Further one-pot transformation as described below also confirmed (−)-alcohol **3** to have *R*-configuration.



(3)

One-Pot Transformation of 1,1,1-Trifluoro-3-(phenylthio)propan-2-ol. One-pot transformation of the resolved alcohol was conducted without isolating intermediate, 1,1,1-trifluoro-2,3-epoxypropane **4**, on treatment with trimethyloxonium tetrafluoroborate–potassium hexamethyldisilazanide (KHMDS). The subsequent reaction with Grignard regents in the presence of a catalytic amount of copper(I) iodide[8] gave arylated products **5a,b** in high enantiomeric excess. Introduction of an azido group was also conducted with sodium azide to give the corresponding azide **6**, which was reported to be converted into the corresponding amino derivative via hydrogenation.[3a] These results show that 1,1,1-trifluoro-3-(phenylthio)propan-2-ol **3** can serve as latent epoxide **4** in useful functional group transformations.

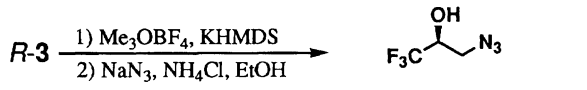


(4)

Table 1. Kinetic Resolution of Ester **2**[a]

Entry	**2**:R	Solv.	Time/h	Yield of **2**/%[c]	Ee/%[d]	Yield of **3**/%[c]	Ee/%[d]	E[e]
1	**a**:H[b]	Acetone	2	46	57	41	56	6
2	**b**:CH_3	Acetone	19	46	88	44	>99	82
3	**b**:CH_3	THF	50	45	95	51	94	118
4	**c**:C_2H_5	THF	73	39	68	26	97	137
5	**c**:C_2H_5	Acetone	29	48	95	44	>99	206

a) The reaction was carried out according to the typical experimental procedure. b) The reaction at room temperature. c) Isolated yield. d) Determined by GLC analysis using chiral stationary column (Chiraldex G-TA, 20 m) after transformation into acetate **2b**; for determination of the absolute configuration, see text. e) See Ref. 11.



6, 51%, 99% ee (5)

Conclusion

In the present study, 1,1,1-trifluoro-3-(phenylthio)propan-2-ol was resolved in high enantiomeric purity by lipase-mediated hydrolysis of the corresponding propinate, and the resolved alcohol was readily transformed into 1,1,1-trifluoro-2,3-epoxypropane. Moreover, arylation and azidation were carried out via in situ formation of 1,1,1-trifluoro-2,3-epoxypropane, giving good derivatives for the preparation of useful chiral materials involving liquid crystals. The resolved *S*-ester (*S*-**2**) could also be hydrolyzed readily into *S*-alcohol (*S*-**3**) without affecting its enantiomeric purity, providing the resolved alcohols in both enantiomeric forms in high enantiomeric purity. Since the preparation of the starting material was readily carried out by the addition of (phenylthio)methyllithium prepared via deprotonation of thioanisole with *n*-BuLi in the presence of DABCO with ethyl trifluoroacetate, followed by reduction with sodium borohydride,[9] the present procedure offers a convenient route to this useful class of compounds.

Experimental

General. Infrared spectra were determined on a JASCO IR-810 spectrometer. ^{1}H NMR spectra were taken on a JEOL JNM-EX270 or JNM-PMX60SI spectrometer using tetramethylsilane as an internal standard. ^{19}F NMR spectra were recorded on Hitachi R-24F spectrometer using $CFCl_3$ as an internal standard. Gas liquid chromatography (GLC) was performed on a Hitachi G-3000 instrument using chiral stationary column (Chiraldex G-TA, 20 m). High-performance liquid chromatography (HPLC) was carried out on a Hitachi L-4000 detector and a Hitachi L-6000 pump using a Finepak SIL column (Merck) or a chiral stationary column (Daicel OJ). Optical rotations were measured with a Union PM-101 polarimeter. Exact mass spectra were taken on a JEOL JMS-DX303-HF spectrometer. Tetrahydrofuran (THF) was freshly distilled from sodium diphenylketyl immediately before use. Dichloromethane was distilled from CaH_2 and stored over molecular sieves 4A. Methanol was distilled from Mg and stored over molecular sieves 4A. Pyridine was pretreated with potassium hydroxide, distilled from CaH_2, and stored over molecular sieves 4A. Acetone was pretreated with $KMnO_4$, distilled, and stored over molecular sieves 3A. TLC plates were prepared with Merck Silica gel 60 PF_{254}. Flash column chromatography was carried out with Merck Silica gel 60.

1,1,1-Trifluoro-3-(phenylthio)propan-2-one (1(R^1=CH_2SPh)): To a mixture of DABCO (1.2 g, 10.6 mmol) and thioanisole (1.20 mL, 10.6 mmol) in THF (15 mL) was added *n*-BuLi (1.66 equiv amount, 6.40 mL, 10.6 mmol) at 0 °C, and the mixture was stirred for 1 h. To the resulting (phenylthio)methyllithium[7] was added a solution of ethyl trifluoroacetate (1.26 mL, 10.26 mmol) in THF (5 mL) at −90 °C. The mixture was stirred at −70 °C for 1 h and then at 0 °C for 3 h. Saturated NH_4Cl (10 mL) was added, and the entire mixture was extracted with ether (10 mL×3). After drying (Na_2SO_4) and concentration of the combined extracts, purification of the crude product by flash silica-gel column chromatography gave 1,1,1-trifluoro-3-(phenylthio)propan-2-one (1.50 g, 67%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ=3.91 (s, 2H), 7.23—7.71 (m, 5H); ^{19}F NMR (CCl_4–$CFCl_3$) δ=−77.0 (s); IR ($CHCl_3$) 2950, 2875, 1760, 1600, 1495, 1335, 1140, 1005, 905, 880 cm^{-1}. HRMS Found: *m/z* 220.0122. Calcd for $C_9H_7OF_3S$: M^+, 220.0170. Upon standing, this compound easily underwent hydrate formation.

1,1,1-Trifluoro-3-(phenylthio)propan-2-ol (3): To a solution of ketone **1** (1.50 g, 6.81 mmol) in methanol (15 ml) was added sodium borohydride (137.5 mg, 3.6 mmol) at 0 °C, and the mixture was allowed to stand at room temperature for 15 min. Saturated aqueous NaCl (10 mL) was added, and the whole mixture was extracted with ethyl acetate (10 mL×3). After drying (Na_2SO_4) and concentration of the combined extracts, the crude product was purified by flash silica gel column chromatography to give the title compound (1.29 g, 85%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ= 2.86 (d, 1H, *J*=4.29 Hz), 3.02 (dd, 1H, *J*=14.36 and 10.07 Hz), 3.36 (dd, 1H, *J*=14.36 and 2.81 Hz), 3.94—4.03 (m, 1H), 7.26—7.44 (m, 5H); ^{19}F NMR (CCl_4–$CFCl_3$) δ=−80.0 (d, *J*=6.6 Hz); IR ($CHCl_3$) 3600, 1580, 1480, 1470, 1360, 1295, 1280, 1130, 1000, 870 cm^{-1}. HRMS Found: *m/z* 222.0313. Calcd for $C_9H_9OF_3S$: M^+, 222.0326.

1,1,1-Trifluoro-2-formyloxy-3-(phenylthio)propane (2a): A mixture of formic acid (8.54 mL, 225 mmol) and acetic anhydride (3.40 mL, 36 mmol) was stirred at room temperature for 5 h. To this mixture was added a solution of alcohol **3** (500 mg, 2.27 mmol) in pyridine (10 mL) at 0 °C, and the resulting mixture was allowed to stand at room temperature for 16 h. Water (10 mL) was added, and the entire mixture was extracted with ethyl acetate (10 mL×3). The combined extracts were washed successively with phosphate buffer and sat aq NaCl, and the mixture was dried over Na_2SO_4. Concentration of this crude mixture gave an oil, which was purified on silica-gel TLC to give the title compound as a colorless oil (442 mg, 79%); ^{1}H NMR ($CDCl_3$) δ=3.11 (dd, 1H, *J*=14.68 and 10.07 Hz), 3.30 (dd, 1H, *J*=14.68 and 2.80 Hz), 5.40—5.55 (m, 1H), 7.25—7.43 (m, 5H), 8.06 (s, 1H); ^{19}F NMR (CCl_4–$CFCl_3$) δ=−78.5 (d, *J*=6.6 Hz); IR ($CHCl_3$) 3050, 2960, 1750, 1580, 1480, 1440, 1375, 1280, 1180, 1140, 950 cm^{-1}. HRMS Found: *m/z* 250.0303. Calcd for $C_{10}H_9O_2F_3S$: M^+, 250.0275.

2-Acetoxy-1,1,1-trifluoro-3-(phenylthio)propane (2b): To a solution of alcohol **3** (500 mg, 2.27 mmol) in dichloromethane (30 mL) was added triethylamine (0.96 mL, 6.75 mmol), acetic anhydride (0.64 mL, 6.75 mmol), and 4-(dimethylamino)pyridine (20 mg, 0.16 mmol) successively at 0 °C; the resulting mixture was stirred at 0 °C for 3 h. Sat aq NaCl (10 mL) was added, and the entire mixture was extracted with ethyl acetate (10 mL×3). The combined extracts were dried over Na_2SO_4. Concentration of the crude mixture gave an oil, which was purified by silica-gel column chromatography to give the title compound as a colorless oil (574 mg, 97%); ^{1}H NMR ($CDCl_3$) δ=2.04 (s, 3H), 3.14 (dd, 1H, *J*=14.68 and 9.90 Hz), 3.25 (dd, 1H, *J*=14.68 and 3.30 Hz), 5.35—5.50 (m, 1H), 7.23—7.43 (m, 5H); ^{19}F NMR (CCl_4–$CFCl_3$) δ=−78.0 (d, *J*=6.6 Hz); IR ($CHCl_3$) 2925, 1760, 1580, 1460, 1360, 990, 950, 860 cm^{-1}. HRMS Found: *m/z* 264.0424. Calcd for $C_{11}H_{11}O_2F_3S$: M^+, 264.0432.

1,1,1-Trifluoro-3-phenylthio-2-(propionyloxy)propane (2c): To a solution of alcohol **3** (2.00 g, 7.22 mmol) in dichloromethane (30 mL) was added triethylamine (1.50 mL, 10.8 mmol), propionyl chloride (0.80 mL, 9.38 mmol), and 4-(dimethylamino)pyridine (20 mg, 0.16 mmol) successively at 0 °C, and the resulting mixture was stirred at room temperature for 17 h. Sat aq NH_4Cl (15 mL) was added, and the entire mixture was extracted with ethyl acetate (10 mL×3). The combined extracts were dried over Na_2SO_4. Concentration of the crude mixture gave an oil, which was purified by

silica-gel column chromatography to give the compound as a colorless oil (2.13 g, 85%); ^{1}H NMR ($CDCl_3$) δ=1.13.(t, 3H, J=7.58 Hz), 2.03—2.38 (m, 2H), 3.13 (dd, 1H, J=14.51 and 9.90 Hz), 3.25 (dd, 1H, J=14.51 and 3.14 Hz), 5.41—5.48 (m, 1H), 7.22—7.42 (m, 5H); ^{19}F NMR (CCl_4–$CFCl_3$) δ=−78.5 (d, J=6.6 Hz); IR ($CHCl_3$) 2850, 1755, 1580, 1460, 1370, 1280, 1000, 905 cm^{-1}. HRMS Found: *m/z* 278.0574. Calcd for $C_{12}H_{13}O_2F_3S$: M^+, 278.0589.

General Procedure for the Lipase Mediated Asymmetric Hydrolysis: To a solution of 1,1,1-trifluoro-3-phenylthio-2-(propionyloxy)propane **2c** (50 mg, 0.18 mmol) in acetone (5 mL) and phosphate buffer (7.5 mL) was added lipase (Amano PS, 46 mg) at room temperature, and the mixture was stirred at 35 °C for 29 h. Filtration of the reaction mixture through a pad of celite and extraction with chloroform (5 mL×3), followed by drying and concentration of the combined extracts, gave a crude oil, which was separated on preparative silica-gel TLC to give (*R*)-1,1,1-trifluoro-3-(phenylthio)propan-2-ol *R*-**3** (19 mg, 48%, >99% ee, $[\alpha]_D^{23}$ −67.4 (*c* 0.38, $CHCl_3$)) and (*S*)-1,1,1-trifluoro-3-phenylthio-2-(propionyloxy)propane *S*-**2c** (22 mg, 44%, 95% ee, $[\alpha]_D^{23}$ +39.6 (*c* 0.44, $CHCl_3$)). Spectral properties were identical with those of the authentic samples as prepared above. The enantiomeric purity was determined by GLC analysis using a chiral stationary column (Chiraldex G-TA, 20 m) after transformation into acetate **2b**.

(*S*)-1,1,1-Trifluoro-2,3-epoxypropane (*S*-4): Trimethyloxonium tetrafluoroborate (980 mg, 6.62 mmol) was placed in a flask under an argon atmosphere. To it was added a solution of *R*-**3** (1.47 g, 6.62 mmol) in dichloromethane (7 mL), and the mixture was stirred at 30 °C for 20 h. All the solvent was removed in vacuo, and triethylene glycol dimethyl ether (6 mL) was added to the resulting viscous oil. The solution of the resulting sulfonium salt was added dropwise to 60% aq solution of NaOH (10 mL) in a round-bottom flask fitted with a distillation apparatus at 100 °C. The epoxide **4** (408 mg, 55%) distilled at 35—38 °C was collected in a flask cooled at −78 °C. The comparison of the optical rotation value ($[\alpha]_D^{23}$ −12.0 (*c* 0.65, $CHCl_3$)) with that reported indicated that the enantiomeric purity of this compound was 98% ee; ^{1}H NMR (CCl_4) δ=2.85—3.05 (m, 2H), 3.39—3.47 (m, 1H); ^{19}F NMR (CCl_4–$CFCl_3$) δ=−75.0 (d, J=4.6 Hz); IR ($CHCl_3$) 2900, 2805, 1450, 1430, 1290, 1160, 990, 910 cm^{-1}. The spectral properties were identical with those of the authentic sample.[3)]

(*S*)-1,1,1-Trifluoro-3-phenylpropan-2-ol (5a) (General Procedure for the Arylation of 3): Trimethyloxonium tetrafluoroborate (100 mg, 0.67 mmol) was placed in a flask under an argon atmosphere. To it was added a solution of *R*-**3** (100 mg, 0.45 mmol) in dichloromethane (2 mL), and the mixture was stirred at 30 °C for 20 h. All the solvent was removed in vacuo, and THF (2 mL) was added to the resulting viscous oil. To the solution of the resulting sulfonium salt was added dropwise a solution of potassium hexamethyldisilazanide (1.18 ml, 0.5 M in toluene, 0.59 mmol, 1 M=1 mol dm^{-3}) at 0 °C. This resulting mixture was added dropwise to a solution of phenylmagnesium bromide (2.75 ml, 0.97 M in THF, 0.90 mmol) in THF (1 mL) in the presence of copper(I) iodide (85.7 mg, 0.45 mmol) at −20 °C, and the whole was stirred at that temperature for 17 h. Sat aq NH_4Cl (5 mL) was added, and the entire mixture was extracted with ethyl acetate (5 mL×3). The combined extracts were dried over Na_2SO_4. Concentration of the crude mixture gave an oil, which was purified on silica-gel TLC to give the title compound as a colorless oil (52 mg, 60%); $[\alpha]_D^{23}$ −28.2 (*c* 0.88, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ=2.20 (brs 1H), 2.83 (dd, 2H, J=14.2 and 9.9 Hz), 3.01 (dd, 1H, J=14.2 and 3.0 Hz), 4.08—4.17 (m, 1H), 7.13—7.43 (m, 5H); ^{19}F NMR (CCl_4–$CFCl_3$) δ=−81.0 (d, J=6.7 Hz); IR ($CHCl_3$) 3570, 3340, 1580, 1450, 1370, 1290, 1000, 870 cm^{-1}. The spectral properties were identical with those reported.[3a,10)] The enantiomeric purity was determined to be 98% ee by HPLC analysis using a chiral stationary column (Daicel OJ).

(*S*)-1,1,1-Trifluoro-3-[4′-(octyloxy)biphenyl-4-yl]propan-2-ol (5b): The reaction was carried out on a 0.45 mmol scale as in the manner described above using Grignard reagent prepared form 4-bromo-4′-(octyloxy)bipheny and magnesium to give the title compound (69 mg, 38%); $[\alpha]_D^{23}$ −22.6 (*c* 1.37, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ=0.80—1.60 (m, 13H), 1.70—1.85 (m, 2H), 2.25 (brs 1H), 2.83 (dd, 2H, J=14.2 and 10.1 Hz), 3.04 (dd, 1H, J=14.2 and 2.0 Hz), 3.96 (t, 2H, J=6.3 Hz), 4.00—4.19 (m, 1H), 6.80—6.95 (m, 2H), 7.16—7.30 (m, 2H), 7.38—7.55 (m, 4H); ^{19}F NMR (CCl_4–$CFCl_3$) δ=−81.0 (d, J=6.7 Hz); IR ($CHCl_3$) 3600, 2930, 2850, 1605, 1495, 1460, 1380, 1285, 980, 870 cm^{-1}. HRMS Found: *m/z* 394.2144. Calcd for $C_{23}H_{29}O_2F_3$: M^+, 394.2123. The enantiomeric purity was determined to be 98% ee by ^{1}H NMR analysis of the corresponding MTPA ester.

(*S*)-3-Azido-1,1,1-trifluoropropan-2-ol (6): Trimethyloxonium tetrafluoroborate (218 mg, 1.47 mmol) was placed in a flask under an argon atmosphere. To it was added a solution of *R*-**3** (272 mg, 1.23 mmol) in dichloromethane (2 mL), and the mixture was stirred at 30 °C for 20 h. All the solvent was removed in vacuo, and THF (2 mL) was added to the resulting viscous oil. To the solution of the resulting sulfonium salt was added dropwise a solution of potassium hexamethyldisilazanide (3.20 ml, 0.5 M in toluene, 1.60 mmol) at 0 °C, and the mixture was stirred for 30 min. Sodium azie (200 mg, 3.08 mmol), ammonium chloride (165 mg, 3.08 mg), and 80% EtOH (5 mL) were added successively at 0 °C, and the whole was allowed to stand at room temperature for 24 h. Water (10 mL) was added, and the entire mixture was extracted with ether (5 mL×3). The combined extracts were dried over Na_2SO_4. Concentration of the crude mixture gave an oil, which was purified on silica-gel TLC to give the title compound as a colorless oil (97 mg, 51%); $[\alpha]_D^{23}$ +13.2 (*c* 0.40, CH_3OH); ^{1}H NMR ($CDCl_3$) δ=2.80 (brs 1H), 3.48—3.62 (m, 2H), 4.10—4.20 (m, 1H); ^{19}F NMR (CCl_4–$CFCl_3$) δ=−79.0 (d, J=6.5 Hz); IR (neat) 3400, 2100, 1280, 1260, 1180, 1140, 850 cm^{-1}. The spectral properties were identical with those reported.[3a)] The enantiomeric purity was determined to be 99% ee by comparison of the optical rotation values.

Generous gifts of lipase (Amano PS) from Amano Pharmaceutical Co. and (*S*)-1,1,1-trifluoro-2,3-epoxypropane from Japan Energy Co. are gratefully acknowledged. We are also very grateful to Mr. T. Ito of Osaka Municipal Technical Research Institute for the measurements of mass spectra.

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