Supporting Information

Novel Synthesis of α -Trifluoromethylated α -Amino Acid Derivatives from γ -Hydroxy- α -fluoro- α -trifluoromethyl Carboxamides

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Experimental Section

Infrared spectra were recorded with a JASCO FT/IR-350. ^1H NMR spectra were obtained with a Varian GEMINI-2000 (300 MHz). ^{13}C NMR spectra were obtained with a Varian GEMINI-2000 (75 MHz). ^{19}F NMR spectra were obtained with a HITACHI FT-NMR R-90HS (85 MHz). Microanalytical data were provided by the Analysis Center of Chiba University. Electron ionization mass spectrum (EIMS) was measured with a JOEL JMS HX-110A and a JMS 700T spectrometer. Analytical HPLC was performed on a HITACHI L-6000 equipped with a HITACHI L-4000 UV detector or a JASCO PU-980 equipped with a JASCO UV-970 UV detector. Preparative HPLC was also performed on a Japan Analytical Industry LC-908. Specific rotations were measured on a JASCO DIP-370 digital polarimeter. X-Ray crystallographic analysis was performed on a Mac Science MXC 18 diffractometer. Kugelrohr bulb-to-bulb distillation was carried out using a SHIBATA GTO-250RS or a SHIBATA GTO-350RS glass tube oven. The materials used herein were obtained from commercial suppliers (Sigma-Aldrich, Inc., Tokyo Kasei Kogyo Co., Ltd., Wako Pure Chemical Industries Ltd., Kanto Chemical Co., Inc., Nakarai Tesque Inc.). PPDA was supplied from Tokyo Kasei Kogyo Co., Ltd.. 2-Fluoro-3-tosylmethyl-2-trifluoromethyl-4-

pentanolide (**3l**) and 2-fluoro-3-tosylmethyl-2-trifluoromethyl-4-butanolide (**3m**) are prepared on the basis of our previous work.^{1(a)} 2-Fluoro-5-iodo-2-trifluoromethyl-4-pentanolide, 2-fluoro-5-iodo-6-methyl-2-trifluoromethyl-4-heptanolide and 2-fluoro-5-iodo-2-trifluoromethyl-4-octanolide were also prepared according to the procedure of our previous work.^{1(b,c)} Dimethylaluminumanilide was prepared according to the literatures.³ *n*-Butyltitanium triisopropoxid was prepared *in situ* from chlorotitanium triisopropoxide based on the literatures of Clauß^{2(a)} and Reetz^{2(b)}. Methylaluminum phenoxides and aluminum triphenoxide were prepared *in situ* based on the literatures of Maruoka and Yamamoto.³

Preparation of *N*-phenyl-4-hydroxy-2-fluoro-3-tosylmethyl-2-(trifluoromethyl)pentanamide (**1a**).

The preparation of **1a** was based on the literatures.⁴ To a solution of trimethylaluminum (17.2 mL of its *n*-hexane 0.98 *M* solution, 16.8 mmol) in THF (140 mL), aniline (1.54 mL, 16.8 mmol) was added. After being stirred for 20 min, a solution of **3l** (993 mg, 2.8 mmol) in THF (28 mL) was dropwise added to the solution over 6 min. And then the resulting mixture was refluxed on heating for 3 h. The reaction mixture was cooled to room temperature and then was quenched with a 50 mL of 1 *N* HCl aqueous solution. The organic layer was separated and the aqueous layer was extracted with chloroform (5 × 10 mL). The combined organic layers were washed with a 1 *N* HCl aqueous solution (3 × 20 mL) and brine (4 × 20 mL). The organic layers were dried over MgSO₄, and concentrated in vacuo to give a light brown solid (1.31 g), which was separated by flash chromatography on silica gel [eluent: *n*-hexane : ethyl acetate (2~3 : 1)] to give **1a** (989 mg) in 79% yield.

Colorless solid: mp 182-183 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.39 (dd, 3H, *J* = 6.6, 2.5 Hz, CH₃CHCH), 2.71 (d, 1H, *J* = 5.8 Hz, CHOH), 2.46 (s, 3H, *p*-tolyl CH₃), 3.19 (ddt, 1H, *J* = 13.4, 8.7, 2.3 Hz, CHCH(CH₂Ts)CF), 3.59 (dd, 1H, *J* = 15.2, 8.7 Hz, CHCH(H)Ts), 3.71 (dd, 1H, *J* = 15.4, 2.1 Hz, CHCH(H)Ts), 4.52 (quintet like, 1H, *J* = 5.8 Hz, CH₃CH(OH)CH), 7.20 (t, 1H, *J* = 7.4 Hz,

phenyl *H*), 7.33-7.41 (m, 4H, phenyl *H*), 7.46 (d, 2H, $J = 7.4$ Hz, phenyl *H*), 7.78 (d, 2H, $J = 8.2$ Hz, *p*-tolyl *H*), 8.07 (br d, 1H, $J = 5.4$ Hz, FCCONH); IR (KBr) 3504, 3370, 1691, 1602, 1542, 1446, 1282, 1197, 1149, 1118, 1089 749 cm^{-1} . Anal. Calcd for $\text{C}_{20}\text{H}_{21}\text{F}_4\text{NO}_4\text{S}$: C, 53.69; H, 4.73; N, 3.13. Found: C, 53.75; H, 4.71; N, 3.06.

Preparation of *N*-benzyl-4-hydroxy-2-fluoro-3-tosylmethyl-2-(trifluoromethyl)pentanamide (1b).

The preparation of **1b** was based on the literatures.⁵ To a solution of **3l** (992 mg, 2.8 mmol) and 2-hydroxypyridine (134 mg, 1.4 mmol) in THF (56 mL), benzylamine (675 μL , 6.2 mmol) was added. After being stirred for 30 min at room temperature, a 1 *N* HCl aqueous solution (40 mL) was added, and the resulting mixture was extracted with chloroform (1 $\times$ 20 mL then 2 $\times$ 10 mL). The combined organic layers were washed with brine (2 $\times$ 20 mL), dried over MgSO_4 , and concentrated in vacuo to give colorless solid (1.27 g), which was subjected to flash chromatography on silica gel [eluent: *n*-hexane-ethyl acetate (2 : 1)] to give **1b** (1.26 g) in 97% yield.

Colorless crystals: mp 146-147 $^{\circ}\text{C}$; ^1H NMR (300 MHz, CDCl_3) δ 1.28 (dd, 3H, $J = 6.6, 2.3$ Hz, CH_3CHCH), 2.46 (s, 3H, *p*-tolyl CH_3), 2.91 (bs, 1H, CHOH), 3.12 (ddt, 1H, $J = 15.3, 8.0, 2.6$ Hz, $\text{CHCH}(\text{CH}_2\text{Ts})\text{CF}$), 3.56 (dd, 1H, $J = 15.5, 8.0$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.64 (ad, 1H, $J = 15.4, 2.9$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 4.33-4.48 (m, 1H, CH_3CHOH), 4.39 (dd, 1H, $J = 14.7, 5.6$ Hz, $\text{NHCH}(\text{H})\text{Ph}$), 4.48 (dd, 1H, $J = 14.8, 5.9$ Hz, $\text{NHCH}(\text{H})\text{Ph}$), 6.77-6.88 (br s, 1H, CONH), 7.20-7.37 (m, 5H, phenyl *H*), 7.37 (d, 2H, $J = 8.0$ Hz, *p*-tolyl *H*), 7.77 (dd, 2H, $J = 8.2, 1.6$ Hz, *p*-tolyl *H*); IR (KBr) 3512, 3386, 1678, 1533, 1299, 1196, 1138, 1086, 739, 695, 555, 512 cm^{-1} . Anal. Calcd for $\text{C}_{21}\text{H}_{23}\text{F}_4\text{NO}_4\text{S}$: C, 54.66; H, 5.02; N, 3.18. Found C, 54.55; H, 4.93; N, 3.00.

***N*-Benzyl-4-hydroxy-2-fluoro-3-tosylmethyl-2-(trifluoromethyl)butanamide (1d).**

1d was prepared from **3m** (409 mg, 1.2 mmol) according to the same procedure described for **1b**. By recrystallization of the crude mixture from *n*-hexane-chloroform, **1d** (507 mg) was obtained in

94% yield.

Colorless crystals: mp 154-155 °C; ^1H NMR (300 MHz, CDCl_3) δ 2.38 (t, 1H, $J = 6.7$ Hz, CH_2OH), 2.47 (s, 3H, p -tolyl CH_3), 3.01 (ddq, 1H, $J = 12.9, 10.2, 2.6$ Hz, $\text{CH}_2\text{CH}(\text{CH}_2\text{Ts})\text{CF}$), 3.50 (dm, 1H, $J = 14.7$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.73 (dd, 1H, $J = 14.7, 10.4$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.98-4.06 (m, 1H, $\text{CHCH}(\text{H})\text{OH}$: after D_2O treatment; δ 4.02, dm, $J = 13.5$ Hz), 4.20-4.30 (m, 1H, $\text{CHCH}(\text{H})\text{OH}$: after D_2O treatment; δ 4.24, dt like, $J = 12.2$ Hz), 4.46 (d, 2H, $J = 5.6$ Hz, NHCH_2Ph), 6.81 (br s, 1H, CONHCH_2), 7.24-7.36 (m, 5H, phenyl H), 7.39 (d, 2H, $J = 8.0$ Hz, p -tolyl H), 7.78 (d, 2H, $J = 8.2$ Hz, p -tolyl H); IR (KBr) 3506, 3332, 1676, 1542, 1303, 1255, 1195, 1132, 1087, 746, 698, 523 cm^{-1} . Anal. Calcd for $\text{C}_{20}\text{H}_{21}\text{F}_4\text{NO}_4\text{S}$: C, 53.69; H, 4.73; N, 3.13. Found: C, 53.41; H, 4.78; N, 3.09.

Preparation of *N*-(4-methoxyphenyl)-4-hydroxy-2-fluoro-3-tosylmethyl-2-(trifluoromethyl)-pentanamide (1c).

A mixture of **3l** (107 mg, 0.30 mmol) and p -anisidine (81.6 mg, 0.66 mmol) was placed in a 20 mL test tube, which was equipped with a screw cap, and heated at 100 °C under nitrogen atmosphere. After 24 h, the reaction mixture was chromatographed on silica gel [eluent: n -hexane-ethyl acetate (2 : 1)] to remove a tar. The eluted mixture was again dissolved in ethyl acetate (30 mL) and washed with a 1 N HCl aqueous solution (3×10 mL) and brine (1×10 mL). The organic layers were dried over MgSO_4 and concentrated to give colorless crystals (125 mg), which was chromatographed on silica gel [eluent: n -hexane-ethyl acetate (2 : 1)] to give **1c** (125 mg) in 93% yield.

Colorless crystals: mp 174-175 °C; ^1H NMR (300 MHz, CDCl_3) δ 1.38 (dd, 3H, $J = 6.6, 2.3$ Hz, CH_3CHCH), 2.46 (s, 3H, p -tolyl CH_3), 2.74 (d, 1H, $J = 6.2$ Hz, CHOH), 3.18 (ddt like, 1H, $J = 13.7, 8.8, 2.5$ Hz, $\text{CHCH}(\text{CH}_2\text{Ts})\text{CF}$), 3.60 (dd, 1H, $J = 15.5, 8.6$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.71 (dd, 1H, $J = 15.6, 2.1$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.80 (s, 3H, p -anisidyl OCH_3), 4.50 (quintet like, 1H, $J = 6.0$ Hz, $\text{CH}_3\text{CH}(\text{OH})\text{CH}$), 6.87 (dd, 2H, $J = 6.9, 2.1$ Hz, p -anisidyl H), 7.36 (d, 2H, $J = 8.9$ Hz, p -tolyl H),

7.37 (t, 2H, $J = 5.8$ Hz, *p*-anisidyl *H*), 7.78 (d, 2H, $J = 8.2$ Hz, *p*-tolyl *H*), 7.98 (br d, 1H, $J = 5.4$ Hz, CFCONHPh); IR (KBr) 3514, 3330, 1693, 1548, 1512, 1283, 1250, 1190, 1141, 1106, 1035, 813 cm^{-1} . Anal. Calcd for $\text{C}_{20}\text{H}_{21}\text{F}_4\text{NO}_4\text{S}$: C, 52.83; H, 4.86; N, 2.93. Found: C, 52.67; H, 4.81; N, 2.86.

***N*-(4-Methoxyphenyl)-4-hydroxy-2-fluoro-3-tosylmethyl-2-(trifluoromethyl)butanamide (1e).**

1e was prepared from **3m** (170 mg, 0.50 mmol) according to the same procedure described for **1c**. **1e** (224 mg) was obtained in 97% yield.

Colorless crystals: mp 149-150 °C; ^1H NMR (300 MHz, CDCl_3) δ 2.38 (t, 1H, $J = 6.4$ Hz, CHOH), 2.47 (s, 3H, *p*-tolyl CH_3), 3.08 (ddq, 1H, $J = 13.1, 10.2, 2.9$ Hz, $\text{CHCH}(\text{CH}_2\text{Ts})\text{CF}$), 3.54 (d like, 1H, $J = 13.3$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.77 (dd, 1H, $J = 14.8, 10.1$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.80 (s, 3H, *p*-anisidyl OCH_3), 4.06-4.16 (m, 1H, $\text{CHCH}(\text{H})\text{OH}$; δ 4.10, d, $J = 12.1$ Hz on treatment with D_2O), 4.28-4.36 (m, 1H, $\text{CHCH}(\text{H})\text{OH}$; δ 4.29, dt like, $J = 12.2$ Hz on treatment with D_2O), 6.88 (dd, 2H, $J = 6.9, 2.1$ Hz, *p*-anisidyl *H*), 7.38 (d, 2H, $J = 8.4$ Hz, *p*-tolyl *H*), 7.79 (d, 2H, $J = 8.4$ Hz, *p*-tolyl *H*), 8.00 (br d, 1H, $J = 5.8$ Hz, CONH(*p*-anisidyl)); IR (KBr) 3497, 3313, 1685, 1599, 1514, 1302, 1251, 1194, 1146, 1087, 1034, 825 cm^{-1} . Anal. Calcd for $\text{C}_{20}\text{H}_{21}\text{F}_4\text{NO}_5\text{S}$: C, 51.83; H, 4.57; N, 3.01. Found: C, 51.54; H, 4.54; N, 2.95.

Preparation of *N*-benzyl-4-hydroxy-2-fluoro-3-methyl-2-(trifluoromethyl)pentanamide (1f).

The desulfonylation of **1b** was performed by a modified procedure of the conventional method.⁶

To a mixture of **1b** (554 mg, 1.2 mmol), Na_2HPO_4 (1.703 g, 12 mmol) and ethanol (704 μL , 12 mmol) in THF (12 mL) was portionwise added sodium (198 mg) at -45 °C (MeCN-CO_2). The reaction mixture was stirred for 6 h at the same temperature. Then, the reaction mixture was warmed to 0 °C and was quenched with a NH_4Cl saturated aqueous solution (10 mL). The resulting mixture was extracted with ethyl acetate (3×10 mL). The organic layers were washed with a 1 *N* HCl aqueous solution (1×10 mL) and brine (4×10 mL), dried over MgSO_4 , and concentrated in

vacuo to give a pale yellow oil (356 mg). This oil was chromatographed on silica gel [eluent: *n*-hexane-ethyl acetate (2 : 1)] to give **1f** (348 mg) in 94% yield.

Colourless crystals: mp 90-94 °C; bp 159 °C/1.4 mmHg (short-path distillation); ¹H NMR (300 MHz, CDCl₃) δ 1.08 (d, 3H, *J* = 7.1 Hz, CH₃CHC), 1.19 (dd, 3H, *J* = 6.2, 1.0 Hz, CH₃CHCH), 1.66 (bs, 1H, CH₃CH(OH)CH), 2.72 (dq, 1H, *J* = 32.6, 7.1, 4.1 Hz, CH₃CHCF), 4.41 (m, 1H, CH₃CH(OH)CH), 4.50 (dd, 1H, *J* = 14.9, 5.7 Hz, NHCH(H)Ph), 4.56 (dd, 1H, *J* = 14.8, 5.7 Hz, NHCH(H)Ph), 6.76 (br s, 1H, CONH), 7.26-7.40 (m, 5H, phenyl *H*); IR (KBr) 3460, 3225, 3248, 1678, 1543, 1441, 1294, 1192, 1155, 1020, 966, 702 cm⁻¹. Anal. Calcd for C₁₄H₁₇F₃NO₂: C, 54.72; H, 5.58; N, 4.56. Found: C, 54.75; H, 5.74; N, 4.41.

***N*-(4-Methoxyphenyl)-4-hydroxy-2-fluoro-3-methyl-2-(trifluoromethyl)pentanamide (1g).**

1g was prepared from **1c** (448 mg, 1.0 mmol) according to the same procedure described for **1f**. **1g** (270 mg) was obtained in 84% yield.

Colorless amorphous solid: mp 112-115 °C (sublimation started at 105-107 °C); ¹H NMR (300 MHz, CDCl₃) δ 1.15 (d, 3H, *J* = 7.1 Hz, CH₃CHCF), 1.24 (dd, 3H, *J* = 6.3, 1.2 Hz, CH₃CHCH), 1.59 (d, 1H, *J* = 4.0 Hz, CHOH; disappeared on treatment with D₂O), 2.76 (dq, 1H, *J* = 32.5, 7.0, 4.4 Hz, CH₃CHCF), 3.81 (s, 3H, *p*-anisidyl OCH₃), 4.26 (sextet like, 1H, *J* = 5.5 Hz, CH₃CH(OH)CH; quintet, *J* = 5.6 Hz on treatment with D₂O), 6.90 (dd, 2H, *J* = 6.7, 2.2 Hz, *p*-anisidyl *H*), 7.46 (dd, 2H, *J* = 6.9, 2.2 Hz, *p*-anisidyl *H*), 8.00 (br d, 1H, *J* = 5.4 Hz, CONH(*p*-anisidyl)); δ 8.05, br d like, *J* = 5.4 Hz on treatment with D₂O); IR (KBr) 3552, 3340, 1682, 1541, 1458, 1286, 1244, 1194, 1155, 1036, 989, 825 cm⁻¹. Anal. Calcd for C₁₄H₁₇F₄NO₃: C, 52.01; H, 5.30; N, 4.33. Found: C, 52.06; H, 5.05; N, 4.31.

Preparation of *N*-benzyl-4-hydroxy-2-fluoro-5-iodo-2-trifluoromethyl-4-pentanamide (10h).

This was prepared according to the same procedure described for **1b** from 2-fluoro-5-iodo-2-trifluoromethyl-4-pentanolide. To a solution of 2-fluoro-5-iodo-2-trifluoromethyl-4-pentanolide (781 mg, 2.5 mmol) and 2-hydroxypyridine (119 mg, 1.3 mmol) in THF (40 mL) was added benzylamine (0.60 mL, 5.5 mmol). After being stirred for 1 h at room temperature, a 20 mL of 1 *N* HCl aqueous solution was added and extracted with chloroform (1 × 20 mL, 1 × 10 mL). The combined organic layers were washed with a 1 *N* HCl aqueous solution (2 × 10 mL) and brine (2 × 40 mL), dried over MgSO₄, and concentrated in vacuo to give a pale yellow oil (1.09 g). This oil was chromatographed on silica gel [eluent *n*-hexane-ethyl acetate (2 : 1)] to give **10h** (1.03 g) in 98% yield.

Colorless crystals: mp 92-93 °C; ¹H NMR (300 MHz, CDCl₃) δ 2.27 (td, 1H, *J* = 14.4, 8.8 Hz, OCHCH(H)CF), 2.43-2.67 (m, 2H, CHOH and OCHCH(*H*)CF; δ 2.57 ddd, 1H, *J* = 36.0, 14.8, 2.9 Hz on treatment with D₂O), 3.21-3.27 (m, 1H, ICH(H)CHO; δ 3.24, dd, *J* = 10.5, 6.4 Hz on treatment with D₂O), 3.33-3.39 (m, 1H, ICH(*H*)CHO; δ 3.35, dd, *J* = 10.4, 4.1 Hz on treatment with D₂O), 3.81 (m, 1H, CH₂CH(OH)CH₂), 4.54 (d, 2H, *J* = 5.9 Hz, NHCH₂Ph), 6.92 (br s, 1H, CONHCH₂), 7.26-7.41 (m, 5H, phenyl *H*); IR (KBr) 3537, 3336, 1668, 1547, 1286, 1230, 1192, 1163, 1146, 692 cm⁻¹. Anal. Calcd for C₁₃H₁₄F₄INO₂: C, 37.25; H, 3.37; N, 3.34. Found: C, 37.43; H, 3.33; N, 3.31.

***N*-Benzyl-4-hydroxy-2-fluoro-5-iodo-6-methyl-2-(trifluoromethyl)heptenamide (10i).**

This was prepared from 2-fluoro-5-iodo-6-methyl-2-trifluoromethyl-4-heptanolide (426 mg, 1.2 mmol) according to the same procedure described above. **10i** (512 mg) was obtained in 92% yield.

Pale yellow crystals: mp 83-84 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.00 (d, 3H, *J* = 6.6 Hz, CH₃(CH₃)CH), 1.06 (d, 3H, *J* = 6.5 Hz, CH₃(CH₃)CH), 1.68 (octet, 1H, *J* = 6.6 Hz, CH₃(CH₃)CHCH), 2.28 (td, 1H, *J* = 14.7, 9.6 Hz, OCHCH(H)CF), 2.74 (ddd, 1H, *J* = 36.6, 15.1,

2.2 Hz, OCHCH(*H*)CF), 3.54-3.59 (m, 1H, CHCH(OH)CH₂), 4.12 (dd, 1H, *J* = 6.8, 5.4 Hz, CHCHICH), 4.56 (d, 2H, *J* = 5.9 Hz, NHCH₂Ph), 6.92 (br s, 1H, CONH), 7.27-7.40 (m, 5H, phenyl *H*); IR (KBr) 3477, 3384, 1689, 1543, 1454, 1200, 1140, 1088, 725 cm⁻¹. Anal. Calcd for C₁₆H₂₀F₄INO₂: C, 41.67; H, 4.37; N, 3.04. Found: C, 41.97; H, 4.53; N, 3.00.

***N*-Benzyl-4-hydroxy-2-fluoro-5-iodo-2-(trifluoromethyl)octanamide (10j).**

This was prepared from 2-fluoro-5-iodo-2-trifluoromethyl-4-octanolide (1.06 g, 3.0 mmol) according to the same procedure described above. **10j** (1.27 g) was obtained in 92% yield by chromatography on silica gel [eluent: *n*-hexane-ethyl acetate (4 : 1)] followed by recrystallization from *n*-hexane-chloroform.

Colorless crystals: mp 92-93 °C; ¹H NMR (300 MHz, CDCl₃) δ 0.94 (t, 3H, *J* = 7.1 Hz, CH₃CH₂), 1.33-1.46 (m, 1H, CH₂CH(*H*)CHI), 1.52-1.79 (m, 2H, CH₃CH₂CH₂), 1.78-1.89 (m, 1H, CH₂CH(*H*)CHI), 2.22-2.34 (m, 2H, CHOH and OCHCH(*H*)CF), 3.34-3.41 (m, 1H, CHCH(OH)CH₂), 4.28 (dt, 1H, *J* = 10.2, 3.6 Hz, CH₂CHICH), 4.56 (d, 2H, *J* = 5.6 Hz, NHCH₂Ph), 6.90 (br s, 1H, NHCH₂Ph), 7.24-7.41 (m, 5H, phenyl *H*); IR (KBr) 3546, 3354, 2956, 1672, 1541, 1290, 1194, 1140, 1122, 700 cm⁻¹. Anal. Calcd for C₁₆H₂₀F₄INO₂: C, 41.67; H, 4.37; N, 3.04. Found: C, 41.73; H, 4.22; N, 2.93.

Preparation of *N*-benzyl-4-hydroxy-2-fluoro-2-(trifluoromethyl)pentanamide (1h).

The preparation of **1h** was based on the literatures.⁷ To a solution of **10h** (629 mg, 1.5 mmol) in THF (20 mL), was added tri(*n*-butyl)tin hydride (0.50 mL, 1.8 mmol) and AIBN (37.9 mg, 0.23 mmol). The reaction mixture was heated at 60 °C for 1.5 h. The resulting reaction mixture was evaporated in vacuo and chromatographed on silica gel [eluent: *n*-hexane-ethyl acetate (3~1 : 1)] to give **1h** (433 mg) in 98% yield.

A colorless oil: bp 160 °C/5.3 mmHg (short-path distillation); ¹H NMR (300 MHz, CDCl₃) δ

1.26 (d, 3H, $J = 6.3$ Hz, CH_3CH), 2.01 (1H, br s, CHOH), 2.15 (ddd, 1H, $J = 15.1, 12.3, 8.9$ Hz, $\text{CHCH}(H)\text{CF}$), 2.46 (ddd, 1H, $J = 37.5, 15.1, 2.3$ Hz, $\text{CHCH}(H)\text{CF}$), 4.04-4.16 (m, 1H, CH_3CHCH_2), 4.52 (dd, 1H, $J = 14.8, 5.8$ Hz, $\text{NHCH}(H)\text{Ph}$), 4.58 (dd, 1H, $J = 14.6, 6.3$ Hz, $\text{NHCH}(H)\text{Ph}$), 6.92 (br s, 1H, CONHPh), 7.25-7.41 (m, 5H, phenyl H); IR (KBr, neat) 3343, 2977, 1682, 1539, 1455, 1433, 1281, 1198, 946, 733, 699, 620 cm^{-1} . Anal. Calcd for $\text{C}_{13}\text{H}_{15}\text{F}_4\text{NO}_2$: C, 53.24; H, 5.16; N, 4.78. Found: C, 53.04; H, 5.17; N, 4.72.

***N*-Benzyl-4-hydroxy-2-fluoro-6-methyl-2-(trifluoromethyl)heptanamide (1i).**

1i was prepared from **10i** (369 mg, 0.80 mmol) according to the same procedure described for **1h**. The purification of the product was performed on silica gel [eluent: *n*-hexane-ethyl acetate (4 : 1)] to give **1i** (256 mg) in 95% yield.

Colorless amorphous solid: mp 69-75 °C; ^1H NMR (300 MHz, CDCl_3) δ 0.89 (t, 6H, $J = 6.5$ Hz, $(\text{CH}_3)_2\text{CH}$), 1.25 (ddd, 1H, $J = 13.6, 8.6, 4.8$ Hz, $\text{CHCH}(H)\text{CHO}$), 1.46 (ddd, 1H, $J = 14.0, 8.5, 5.6$ Hz, $\text{CHCH}(H)\text{CHO}$), 1.73 (octet, 1H, $J = 6.8$ Hz, $(\text{CH}_3)_2\text{CHCH}_2$), 1.83 (m, 1H, $\text{CH}_2\text{CH}(\text{OH})\text{CH}_2$), 2.09 (ddd, 1H, $J = 15.0, 12.2, 9.2$ Hz, $\text{CHCH}(H)\text{CF}$), 2.46 (ddd, 1H, $J = 37.6, 15.3, 2.2$ Hz, $\text{CHCH}(H)\text{CF}$), 3.87-4.00 (m, 1H, $\text{CH}_2\text{CH}(\text{OH})\text{CH}_2$), 4.52 (dd, 1H, $J = 15.2, 6.1$ Hz, $\text{NHCH}(H)\text{Ph}$), 4.58 (dd, 1H, $J = 15.3, 6.5$ Hz, $\text{NHCH}(H)\text{Ph}$), 6.92 (br s, 1H, CONHPh), 7.27-7.40 (m, 5H, phenyl H); IR (KBr) 3452, 3271, 2967, 1667, 1558, 1264, 1197, 1155, 1117, 1030, 697, 618 cm^{-1} . Anal. Calcd for $\text{C}_{16}\text{H}_{21}\text{F}_3\text{NO}_2$: C, 57.31; H, 6.31; N, 4.18. Found: C, 57.04; H, 6.50; N, 4.10.

***N*-Benzyl-4-hydroxy-2-fluoro-2-(trifluoromethyl)octanamide (1j).**

1j was prepared from **10j** (462 mg, 1.0 mmol) according to the same procedure described for **1h**. The purification of the product was performed on silica gel [eluent: *n*-hexane-ethyl acetate (4 : 1)] to give **1j** (333 mg) in 99% yield.

Colorless amorphous solid: mp 50-54 °C (sublimation started at 40-43 °C); ^1H NMR (300 MHz,

CDCl₃) δ 0.90 (t, 3H, J = 7.0 Hz, CH₃CH₂), 1.22-1.56 (m, 6H, CH₃(CH₂)₃CH), 1.89 (m, 1H, CH₂CH(OH)CH₂), 2.11 (ddd, 1H, J = 15.1, 12.4, 9.3 Hz, CHCH(H)CF), 2.47 (ddd, 1H, J = 37.9, 15.1, 1.7 Hz, CHCH(H)CF), 3.79-3.91 (m, 1H, CH₂CH(OH)CH₂), 4.53 (dd, 1H, J = 15.2, 6.0 Hz, NHCH(H)Ph), 4.56 (dd, 1H, J = 15.5, 5.8 Hz, NHCH(H)Ph), 6.91 (br s, 1H, CONHPh), 7.27-7.40 (m, 5H, phenyl H); IR (KBr, neat) 3339, 2956, 2934, 1676, 1543, 1305, 1277, 1197, 1144, 1090, 698, 626 cm⁻¹. Anal. Calcd for C₁₆H₂₁F₄NO: C, 57.31; H, 6.31; N, 4.18. Found: C, 57.35; H, 6.39; N, 4.10.

Preparation of *N*-benzyl-2-fluoro-4-methoxy-3-tosylmethyl-2-(trifluoromethyl)pentanamide (**6**).

6 was prepared from **1b** with trimethyloxonium tetrafluoroborate,⁸ because the methylation of **1b** with methyl iodide was unsuccessful. *n*-Butyllithium (1.22 mL, 1.6 M *n*-hexane solution, 2.0 mmol), was dropwise added to a solution of **1b** (693 mg, 1.5 mmol) in THF (30 mL) at -10 °C. After being stirred for 21 min, trimethyloxonium tetrafluoroborate (231 mg, 1.6 mmol) was added and then the reaction mixture was further stirred at -10 °C for 2 h 40 min. After a 20 mL of saturated NH₄Cl aqueous solution was added, the extraction with chloroform (2 × 10 mL) was performed. The organic layers were washed with a 1 N HCl aqueous solution (1 × 20 mL) and brine (2 × 20 mL), dried over MgSO₄, and concentrated in vacuo to give a pale yellow oil (740 mg). This oil was chromatographed on silica gel [eluent: 1st *n*-hexane–ethyl acetate (3~5 : 1)] to give **6** (191 mg) and **3l** (53 mg) in 27% and 10% yield, respectively, along with **1b** (204 mg; 29% yield)

Colorless crystals: mp 148-149 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.28 (dd, 3H, J = 6.7, 3.0 Hz, CH₃CHCH), 2.46 (s, 3H, *p*-tolyl CH₃), 2.96-3.06 (m, 1H, CHCHCF), 3.13 (s, 3H, OCH₃), 3.44 (dd, 1H, J = 15.5, 8.0 Hz, CHCH(H)Ts), 3.78 (d quintet like, 1H, J = 15.4, 1.3 Hz, CHCH(H)Ts), 3.95 (q, 1H, J = 6.4 Hz, CH₃CHCH), 4.47 (d, 2H, J = 5.8 Hz, NHCH₂Ph), 6.68 (br q, 1H, FCCONHCH₂), 7.19-7.45 (m, 7H, *p*-tolyl H and phenyl H), 7.80 (d, 2H, J = 7.3 Hz, *p*-tolyl H); IR (KBr) 3328, 1688, 1542, 1304, 1288, 1210, 1186, 1146, 1107, 1089, 1038, 647 cm⁻¹. Anal. Calcd for

C₂₂H₂₅F₄NO₄S: C, 55.57; H, 5.30; N, 2.95. Found: C, 55.53; H, 5.47; N, 2.88.

Preparation of *N*-benzyl-2-fluoro-2-(trifluoromethyl)octanamide (**8**).

The preparation of **8** was based on the literatures.⁹ To a solution of **1j** (403 mg, 1.2 mmol) in THF (15 mL), sodium hydride (71.3 mg, 60% in mineral oil, 1.8 mmol) was added at 0 °C, and the reaction mixture was stirred for 10 min. Carbon disulfide (220 µl, 3.7 mmol) was added and after 21 min, methyl iodide (149 µl, 2.4 mmol) was added. The reaction mixture was further stirred for 13 min at 0 °C and was quenched with a 10 mL of saturated NH₄Cl aqueous solution. The resulting mixture was extracted with ether (3 × 10 mL). The organic layers were washed with brine (2 × 10 mL), dried over sodium sulfate and concentrated in vacuo, chromatographed on silica gel [eluent: *n*-hexane-ethyl acetate (6~8: 1)] to give xanthate ester of **1j** (405 mg) in 76% yield. To a solution of the xanthate ester of (380 mg, 0.86 mmol) in toluene (10 mL), tri(*n*-butyl)tin hydride (0.38 mL, 1.4 mmol) and AIBN (60.0 mg, 0.36 mmol) was added. The reaction mixture was heated at 75°C for 3 h 30 min and then evaporated in vacuo. Chromatography of the residue was performed on silica gel [eluent: *n*-hexane-ethyl acetate (8~20:1)] to give **8** (255 mg) in 93% yield.

Colorless solid: mp 48-49 °C; bp 142 °C/6 mmHg (Kugel Rohr distillation); ¹H NMR (300 MHz, CDCl₃) δ 0.88 (t, 3H, CH₃CH₂), 1.13-1.51 (m, 8H, CH₃(CH₂)₄CH₂), 1.89-2.06 (m, 1H, CH₂CH(*H*)CF), 2.28 (dtm, 1H, *J* = 39.2, 13.4 Hz, CH₂CH(*H*)CF), 4.466 (dd, 1H, *J* = 15.1, 5.6 Hz, NHCH(*H*)Ph), 4.468 (dd, 1H, *J* = 15.1, 5.6 Hz, NHCH(*H*)Ph), 6.74 (br s, 1H, CONHCH₂), 7.24-7.41 (m, 5H, phenyl *H*); IR (KBr) 3358, 2931, 1671, 1537, 1306, 1280, 1196, 1149, 1046, 743, 699, 632 cm⁻¹. Anal. Calcd for C₁₆H₂₁F₄NO: C, 60.18; H, 6.63; N, 4.39. Found: C, 60.17; H, 6.76; N, 4.29.

The reaction of **3l** with dimethylaluminum anilide.

To a solution of aniline (149 mg, 1.6 mmol) in THF (20 mL), trimethylaluminum (1.64 mL, 0.98 M *n*-hexane solution, 1.6 mmol) was added at room temperature. After 21 min stirring, a solution of **3l** (142 mg, 0.40 mmol) in THF (5 mL) was added portionwise over 4 min. The reaction mixture was refluxed on heating for 20 h. After a 20 mL of 1 *N* HCl aqueous solution was added, the resulting mixture was extracted with ethyl acetate (3 × 10 mL). The organic layers were washed with a 1 *N* HCl aqueous solution (2 × 10 mL) and brine (3 × 10 mL), dried over MgSO₄, and concentrated in vacuo to give a pale brown foam (206 mg), which was chromatographed on silica gel [eluent: *n*-hexane-ethyl acetate (2~3 : 1)] to give **1a** (32 mg), **2a** (88 mg), and **4a** (21 mg) in 18%, 51%, and 11% yields respectively.

The reaction of **3l** with dimethylaluminumanilide (in shortened reaction time).

To a solution of aniline (149 mg, 1.6 mmol) in THF (20 mL), trimethylaluminum (1.64 mL, 0.98 M *n*-hexane solution, 1.6 mmol) was added at room temperature. After 21 min stirring, a solution of **3l** (142 mg, 0.40 mmol) in THF (5 mL) was added and the reaction mixture was refluxed on heating for 4.5 h. Then, a 10 mL of 1 *N* HCl aqueous solution was added and the resulting mixture was extracted with ethyl acetate (3 × 10 mL). The organic layers were washed with a 1 *N* HCl aqueous solution (2 × 10 mL) and brine (3 × 10 mL), dried over MgSO₄, and concentrated in vacuo to give a pale yellow amorphous solid (172 mg), which was chromatographed on silica gel [eluent: *n*-hexane-ethyl acetate (3 : 1)] to give **1a** (101 mg) in 56% yield together with the unchanged **3l** (40 mg; 28% yield).

2-Phenylamino-3-tosylmethyl-2-trifluoromethyl-4-pentanolide (**2a**).

Colorless needle crystals: mp 171-172 °C (sublimation started at 147-148 °C); ¹H NMR (300 MHz, CDCl₃) δ 1.71 (d, 3H, *J* = 6.5 Hz, CH₃CH), 2.47 (s, 3H, *p*-tolyl CH₃), 3.18 (dd, 1H, *J* = 13.8,

10.4 Hz, CHCH(H)Ts), 3.27 (ddd, 1H, $J = 10.3, 4.7, 1.8$ Hz, CHCHCH₂Ts), 3.47 (dd, 1H, $J = 13.9, 1.6$ Hz, CHCH(H)Ts), 4.38 (s, 1H, CONHPh), 4.92 (dq, 1H, $J = 11.1, 6.3$ Hz, CH₃CHCH), 6.56 (d, 2H, $J = 8.0$ Hz, phenyl *H*), 6.93 (t, 1H, $J = 8.0$ Hz, phenyl *H*), 7.19 (t, 2H, $J = 8.0$ Hz, phenyl *H*), 7.39 (d, 2H, $J = 8.0$ Hz, *p*-tolyl *H*), 7.74 (d, 2H, $J = 8.2$ Hz, *p*-tolyl *H*); ¹³C NMR (75 MHz, CDCl₃) δ 21.10, 22.53, 42.64, 56.68, 68.58 (q, $J=28.1$ Hz, NCCF₃), 82.13, 117.24, 122.60, 127.56 (q, $J = 176.4$ Hz, CF₃), 128.90, 130.50, 131.12, 136.40, 142.93, 146.58, 169.29 (C=O); ¹⁹F NMR (85 MHz, CDCl₃, TFA (-77 ppm)) δ 70.04 (CF₃); IR (KBr) 3377, 1768, 1602, 1498, 1300, 1257, 1176, 1143, 1085, 1063, 754, 558 cm⁻¹. Anal. Calcd for C₂₀H₂₀F₃NO₄S: C, 56.20; H, 4.72; N, 3.28. Found: C, 56.04; H, 4.62; N, 3.15.

5-Methyl-3-phenylamino-2-phenylimino-3-trifluoromethyl-4-(tosylmethyl)oxolane (4a).

Orange solid; mp 202-203 °C; sublimation point 191 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.67 (3H, d, $J = 6.6$ Hz, CH₃CHO), 2.47 (3H, s, *p*-tolyl CH₃), 3.18 (1H, dd, $J = 14.2, 11.2$ Hz, CHCH(H)SO₂), 3.53 (1H, ddd, $J = 11.2, 3.3, 1.5$ Hz, CHCH(H)SO₂), 4.90 (1H, s, NH; disappeared on treatment with D₂O), 4.98 (1H, qd, $J = 6.6, 3.3$ Hz, CH₃CHCH), 6.56 (2H, d, $J = 8.2$ Hz, phenyl *H*), 6.88 (1H, t, $J = 7.4$ Hz, phenyl *H*), 7.18-7.11 (5H, m, phenyl *H*), 7.33 (2H, t like, $J = 7.8$ Hz, phenyl *H*), 7.38 (2H, d, $J = 8.2$ Hz, *p*-tolyl *H*), 7.73 (2H, d, $J = 8.4$ Hz, *p*-tolyl *H*); ¹⁹F NMR (85 MHz, CDCl₃, TFA(-77 ppm)) δ 67.60 (CF₃); IR (KBr) 3355, 1712, 1595, 1499, 1301, 1241, 1214, 1190, 1176, 1148, 1123, 1087, 759 cm⁻¹. Anal. Calcd for C₂₆H₂₁F₃N₂O₃S: C, 62.14; H, 5.01; N, 5.57. Found: C, 61.89; H, 5.16; N, 5.48.

A typical procedure for the reaction of 1b with trimethylaluminum.

To a solution of trimethylaluminum (0.67 mL, 0.98 M *n*-hexane solution, 0.66 mmol) in THF (20 mL), a solution of **1b** (139 mg, 0.30 mmol) in THF (5 mL) was portionwise added over 5 min. The reaction mixture was refluxed on heating for 21 h. And then a 6 mL of 1 N HCl aqueous solution

was added. The resulting mixture was extracted with chloroform (2×20 mL, 2×10 mL). The organic layers were washed with a 1 *N* HCl aqueous solution (2×10 mL) and brine (2×10 mL), dried over MgSO_4 , and concentrated in vacuo to give a yellow oil (131 mg). ^1H NMR analysis using triphenylmethane as an internal standard showed that this oil contained **2b** (90 mg: 68% yield), **3l** (13 mg: 12% yield), and the unchanged **1b** (24 mg: 17% yield). In ^1H NMR spectrum, the obtained **2b** was observed as single diastereomer.

The reaction of the other aluminum reagents with **1b** were performed under the same procedure described above. These results were shown in Table S1.

Table S1. Reaction of **1b** with aluminum reagents

Reaction scheme: **1b** $\xrightarrow[\text{THF, reflux, 21 h}]{\text{"Al" (2.0-2.2 equiv)}}$ **2b** + **3l**

entry	Aluminum Reagent	Yield (%) ^a		
		2b	3l	1b
1	Me_3Al	68	12	17
2	$\text{Me}_2\text{Al}(\text{OPh})$	62	17	12
3	$\text{MeAl}(\text{OPh})_2$	61	24	10
4	$\text{Al}(\text{OPh})_3$	0	72	14
5	$\text{Al}(\text{O}i\text{-Pr})_3$	0	7	87
6	Me_2AlCl	31	33	23
7	<i>i</i> - Bu_2AlH	77	6	0

^a Yields were determined by ^1H NMR using Ph_3CH as an internal standard.

The typical reaction procedure for the reaction of **1a** with trimethylaluminum.

To a solution of trimethylaluminum (0.66 mL, 1.0 M *n*-hexane solution, 0.66 mmol) in THF (20 mL), a solution of **1a** (135 mg, 0.30 mmol) in THF (5 mL) was added portionwise over 6 min. The reaction mixture was refluxed on heating for 21 h. And then a 10 mL of 1 *N* HCl aqueous solution was added. The resulting mixture was extracted with chloroform (1×20 mL, 2×10 mL). The organic layers were washed with a 1 *N* HCl aqueous solution (3×10 mL) and brine (2×10 mL), dried over MgSO_4 , and concentrated in vacuo to give a yellow oil (163 mg). ^1H NMR analysis using

triphenylmethane as an internal standard showed that this oil contained **2a** (83 mg: 69% yield), **3l** (19 mg: 14% yield). In ^1H NMR spectrum, the obtained **2a** was observed as single diastereomer.

Crystal structural data of **2a**: $\text{C}_{20}\text{H}_{20}\text{F}_3\text{NO}_4\text{S}$, MW = 427.43, orthorhombic $Pna2_1$, $a = 26.428(6)$ Å, $b = 6.2508(18)$ Å, $c = 11.841(3)$ Å, $\alpha = 90.00^\circ$, $\beta = 90.00^\circ$, $\gamma = 90.00^\circ$, $V = 1956.1(9)$ Å³, $Z = 4$, $2\theta_{\text{max}} = 60.26^\circ$, $D_{\text{calcd}} = 1.451$ gcm⁻³, $F(000) = 888$, $\mu = 1.976$ mm⁻¹, Cu K α ($\lambda = 1.5418$ Å) radiation at 298 K, 1950 reflections collected, 264 parameters ($R_{\text{int}} = 0.0000$), $R = 0.0344$, $wR = 0.0876$ for reflections with $[I > 2.00 \sigma(I)]$, $S = 1.047$.

ORTEP drawing of **2a** was shown in Figure S1.

Figure S1. ORTEP drawing of **2a**

A typical procedure for the reaction of **1b** with DIBAL-H.

To a solution of DIBAL-H (0.66 mL, 1.0 M *n*-hexane solution, 0.66 mmol) in THF (20 mL), a solution of **1b** (139 mg, 0.30 mmol) in THF (5 mL) was portionwise added over 5 min. After the reaction mixture was refluxed on heating for 21 h, a 10 mL of 1 N HCl aqueous solution was added. And the resulting mixture was extracted with chloroform (3×10 mL). The organic layers were washed with a 1 N HCl aqueous solution (2×10 mL) and brine (2×10 mL), dried over MgSO_4 , and concentrated in vacuo to give a yellow oil (144 mg), which was chromatographed on silica gel [eluent: *n*-hexane-ethyl acetate (2 : 1)] to give colorless foamy solid (116 mg). ^1H NMR analysis using triphenylmethane as an internal standard showed that this solid contained **2b** (104 mg: 78% yield) and **3l** (7 mg: 7% yield). A pure sample of **2b** was obtained by recrystallization from *n*-

hexane-chloroform.

Colorless solid; mp 112-113 °C; ^1H NMR (300 MHz, CDCl_3) δ 1.72 (d, 3H, $J = 6.2$ Hz, CH_3CH), 1.91 (dd, 1H, $J = 9.3, 4.5$ Hz, NHCH_2Ph), 2.47 (s, 3H, p -tolyl CH_3), 3.02 (td, 1H, $J = 8.8, 2.1$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.18 (dd, 1H, $J = 14.6, 9.1$ Hz, CHCHCH_2Ts), 3.59 (dd, 1H, $J = 14.6, 2.2$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.71 (dd, 1H, $J = 12.2, 9.5$ Hz, $\text{NHCH}(\text{H})\text{Ph}$), 3.85 (dd, 1H, $J = 12.3, 4.5$ Hz, $\text{NHCH}(\text{H})\text{Ph}$), 4.64 (dq, 1H, $J = 8.4, 6.1$ Hz, CH_3CHCH), 7.20-7.27 (m, 2H, phenyl H), 7.28-7.32 (m, 3H, phenyl H), 7.40 (d, 2H, $J = 8.3$ Hz, p -tolyl H), 7.77 (d, 2H, $J = 8.2$ Hz, p -tolyl H); IR (neat) 3339, 2930, 1779, 1597, 1495, 1454, 1303, 1147, 1088, 816, 743, 557 cm^{-1} . Anal. Calcd for $\text{C}_{21}\text{H}_{22}\text{F}_3\text{NO}_4\text{S}$: C, 57.14; H, 5.02; N, 3.17. Found: C, 57.00; H, 5.04; N, 3.08.

2-Hydroxy-3-benzylamino-3-trifluoromethyl-4-tosylmethyl-5-methyloxolane (**5b**).

By the reaction of **1b** (138 mg, 0.30 mmol) with 3.2 mol-equiv. of DIBAL-H, **5b** (39 mg: 30% yield) was obtained as a mixture of two diastereomers.

A colorless oil: ^1H NMR (300 MHz, CDCl_3) (major diastereomer) δ 1.24 (d, 3H, $J = 6.2$ Hz, CH_3CH), 2.46 (s, 3H, p -tolyl CH_3), 2.47 (td, 1H, $J = 8.3, 2.7$ Hz, $\text{CHCHCH}(\text{H})\text{Ts}$), 2.84 (dd, 1H, $J = 14.8, 2.7$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.35 (br dd like, $J = 11.1, 3.0$ Hz, NHCH_2Ph ; disappeared on treatment with D_2O), 3.70 (t, 1H, $J = 12.2$ Hz, $\text{NHCH}(\text{H})\text{Ph}$), 3.77 (dd, 1H, $J = 14.8, 9.3$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 4.00 (quintet, 1H, $J = 6.5$ Hz, CH_3CHCH), 4.05 (br d, 1H, $J = 12.4$ Hz, $\text{NHCH}(\text{H})\text{Ph}$), 4.29 (d, 1H, $J = 3.8$ Hz, OCHOH ; disappeared on treatment with D_2O), 5.62 (d, 1H, $J = 2.6$ Hz, $\text{OCH}(\text{OH})$), 7.21-7.40 (m, 7H, phenyl H & p -tolyl H), 7.71 (d, 2H, $J = 8.2$ Hz, p -tolyl H). (minor diastereomer) δ 1.58 (d, 3H, $J = 6.2$ Hz, CH_3CH), 2.97 (td, 1H, $J = 8.5, 2.8$ Hz, $\text{CHCHCH}(\text{H})\text{Ts}$), 3.05 (dd, 1H, $J = 13.7, 8.6$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.45 (dd, 1H, $J = 14.0, 2.7$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.86 (br s, 1H, OCHOH ; disappeared on treatment with D_2O), 4.22 (quintet like, 1H, $J = 6.6$ Hz, CH_3CHCH), 5.50 (s, 1H, $\text{OCH}(\text{OH})$), 7.88 (d, 2H, $J = 8.2$ Hz, p -tolyl H). The other signals of the minor diastereomer was overlapped with the signals of the major diastereomer.; IR

(KBr) 3447, 3323, 2976, 2929, 1791(w), 1597, 1302, 1289, 1148, 1086, 1045, 561 cm^{-1} ; LRMS (EI, 70 eV) 443 (M^+ , 0.95), 440 (0.96), 352 (2.28), 306 (17.7), 242 (17.1), 212 (1.30), 196 (4.04), 157 (5.87), 150 (12.0), 139 (6.16), 106 (29.7), 91 (100), 65 (4.20), 55 (2.20). Anal. Calcd. for $\text{C}_{21}\text{H}_{24}\text{F}_3\text{NO}_4\text{S} + 0.15 \text{ H}_2\text{O}$: C, 56.53; H, 5.49; N, 3.14. Found: C, 56.53; H, 5.43; N, 2.97.

A typical procedure for the reaction of **1a** with DIBAL-H.

To a solution of DIBAL-H (0.63 mL, 1.0 M *n*-hexane solution, 0.63 mmol) in THF (20 mL), a solution of **1a** (129 mg, 0.29 mmol) in THF (5 mL) was portionwise added over 4 min and the reaction mixture was refluxed on heating for 21 h. Then a 10 mL of 1 N HCl aqueous solution was added. And the resulting mixture was extracted with chloroform ($3 \times 10 \text{ mL}$). The organic layer was washed with a 1 N HCl aqueous solution ($2 \times 10 \text{ mL}$) and brine ($2 \times 10 \text{ mL}$), dried over MgSO_4 , and concentrated in vacuo to give an orange oil (129 mg), which was chromatographed on silica gel [eluent: *n*-hexane-ethyl acetate (2 : 1)] to give colorless foamy solid (107 mg). ^1H NMR analysis using triphenylmethane as an internal standard showed that this solid contained **2a** (71 mg: 58% yield) and **3l** (32 mg: 31% yield). A pure sample of **2a** was obtained by recrystallization from *n*-hexane-chloroform.

The reaction of **6** with 2.2 equiv of DIBAL-H.

To a solution of DIBAL-H (0.66 mL, 1.0 M *n*-hexane solution, 0.66 mmol) in THF (20 mL), a solution of **6** (143 mg, 0.30 mmol) in THF (5 mL) was portionwise added over 3 min and the reaction mixture was refluxed on heating for 21 h. Then, a 10 mL of 1 N HCl aqueous solution was added, and the resulting mixture was extracted with chloroform ($3 \times 10 \text{ mL}$). The organic layers were washed with a 1 N HCl aqueous solution ($3 \times 10 \text{ mL}$) and brine ($2 \times 10 \text{ mL}$), dried over MgSO_4 , and concentrated in vacuo to give a yellow oil (141 mg). This oil was chromatographed on silica gel [eluent: *n*-hexane-ethyl acetate (3 : 1)] to give **7** (21.8 mg: 20% yield) along with **6** (94.8

mg: 66% yield). The ratio of two diastereomers of **7** was determined to be 7 : 3 by ^1H NMR analysis.

3-Fluoro-2-hydroxy-5-methyl-4-tosylmethyl-3-(trifluoromethyl)oxolane (7 : 3 diastereomeric mixture) (7).

Colorless crystals: mp 127-129°C (sublimation started at 119°C); ^1H NMR (300 MHz, CDCl_3) (major isomer) δ 1.56 (t, 3H, $J = 6.2$ Hz, $\text{OCH}(\text{CH}_3)\text{CH}$), 2.48 (s, 3H, p -tolyl CH_3), 2.67 (ddt like, 1H, $J = 29.9, 12.0, 3.4$ Hz, CHCHCH_2Ts), 2.91 (t, 1H, $J = 2.7$ Hz, OCHOH), 3.36 (d like, 1H, $J = 12.8$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 3.48 (t like, 1H, $J = 13.1$ Hz, $\text{CHCH}(\text{H})\text{Ts}$), 4.80 (quintet like, 1H, $J = 6.1$ Hz, CH_3CHCH), 5.52 (dd, 1H, $J = 6.7, 3.0$ Hz, OCHOH), 7.40 (d, 2H, $J = 8.7$ Hz, p -tolyl H), 7.80 (d, 2H, $J = 8.5$ Hz, p -tolyl H). (minor isomer) δ 1.61 (dd like, 1H, $J = 6.3$ Hz, $\text{OCH}(\text{CH}_3)\text{CH}$), 5.38 (dd, 1H, $J = 6.7, 3.0$ Hz, OCHOH), 7.41 (d, 2H, $J = 8.7$ Hz, p -tolyl H). The other signals of the minor diastereomer was overlapped with the signals of the major diastereomer.; IR (KBr) : 3509, 1307, 1280, 1195, 1152, 1135, 1085, 1077, 1062, 1028, 653, 553 cm^{-1} . Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{F}_4\text{O}_4\text{S}$: C, 47.19; H, 4.53. Found: C, 47.43; H, 4.36.

The reaction of 8 with 1.1 equiv of DIBAL-H.

To a solution of DIBAL-H (0.66 mL, 1.0 M n -hexane solution, 0.66 mmol) in THF (20 mL), a solution of **8** (192 mg, 0.60 mmol) in THF (5 mL) was portionwise added over 3 min and the reaction mixture was refluxed on heating for 21 h. Then, after chloroform (20 mL) was added, the resulting solution was washed with a 1 N HCl aqueous solution (3×20 mL), a saturated NaHCO_3 solution (1×10 mL), and brine (2×10 mL). The organic layer was dried over MgSO_4 , and concentrated in vacuo to give a yellow oil (190 mg), which was chromatographed on silica gel [eluent: n -hexane-ethyl acetate (10 : 1)] to give the unchanged **8** (177 mg; 92% yield).

A typical procedure for the reaction of **1** (except for **1a** and **1b**) with DIBAL-H.

To a solution of DIBAL-H (0.66 mL, 1.0 M *n*-hexane solution, 0.66 mmol) in THF (20 mL), a solution of **1c** (134 mg, 0.30 mmol) in THF (5 mL) was portionwise added over 4 min and the reaction mixture was refluxed on heating for 21 h. After a 10 mL of 1 *N* HCl aqueous solution was added, the resulting mixture was extracted with chloroform (3 × 10 mL). The organic layers were washed with a 1 *N* HCl aqueous solution (2 × 10 mL) and brine (2 × 10 mL), dried over MgSO₄, and concentrated in vacuo to give an orange oil (153 mg), which was chromatographed on silica gel [eluent: *n*-hexane-ethyl acetate (2 : 1)] to give **2c** (108 mg; 80% yield).

Colorless crystals: mp 166-167 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.66 (d, 3H, *J* = 6.3 Hz, CH₃CH₂), 2.48 (s, 3H, *p*-tolyl CH₃), 3.13 (ddd, 1H, *J* = 10.0, 6.5, 1.5 Hz, CHCHCH₂Ts), 3.21 (dd, 1H, *J* = 13.8, 9.4 Hz, CHCH(H)Ts), 3.60 (dd like, 1H, *J* = 13.7, 1.2 Hz, CHCH(H)Ts), 3.77 (s, 3H, *p*-anisidyl OCH₃), 4.58 (quintet, 1H, *J* = 6.2 Hz, CH₃CHCH), 3.94 (s, 1H, *p*-anisidyl NH), 6.72 (dd like, 2H, *J* = 6.5, 2.8 Hz, *p*-anisidyl *H*), 6.77 (dd like, 2H, *J* = 6.5, 2.8 Hz, *p*-anisidyl NH), 7.40 (d, 2H, *J* = 8.1 Hz, *p*-tolyl *H*), 7.78 (d, 2H, *J* = 8.4 Hz, *p*-tolyl *H*); IR (KBr) 3386, 1773, 1513, 1302, 1247, 1222, 1196, 1182, 1171, 1143, 1087, 560 cm⁻¹. Anal. Calcd for C₂₁H₂₂F₄NO₅S: C, 55.14; H, 4.85; N, 3.06. Found: C, 55.14; H, 4.83; N, 3.06.

2-Benzylamino-2-trifluoromethyl-3-tosylmethyl-4-butanolide (**2d**).

Similarly treatment of **1d** (134 mg, 0.30 mmol) with DIBAL-H (0.66 mmol) in THF gave **2d** (82 mg; 64% yield) along with **3m** (10 mg; 10% yield).

Colorless crystals: mp 158-159 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.83 (t, 1H, *J* = 7.1 Hz, NHCH₂Ph), 2.47 (s, 3H, *p*-tolyl CH₃), 3.18 (dd, 1H, *J* = 13.7, 11.1 Hz, CHCH(H)Ts), 3.33-3.39 (m, 1H, CHCHCH₂Ts), 3.45 (dd, 1H, *J* = 13.5, 1.9 Hz, CHCH(H)Ts), 3.83 (dd, 1H, *J* = 15.9, 6.6 Hz, NHCH(H)Ph), 3.87 (dd, 1H, *J* = 16.8, 6.2 Hz, NHCH(H)Ph), 4.41 (dd, 1H, *J* = 9.6, 7.4 Hz, OCH(H)CH), 4.77 (dd, 1H, *J* = 9.8, 7.1 Hz, OCH(H)CH), 7.23-7.34 (m, 5H, phenyl *H*), 7.39 (d, 2H,

$J = 8.0$ Hz, *p*-tolyl H), 7.76 (d, 2H, $J = 8.1$ Hz, *p*-tolyl H); IR (KBr) 3346, 1780, 1310, 1276, 1246, 1181, 1145, 1090, 1016, 978, 695, 560 cm^{-1} . Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{F}_3\text{NO}_4\text{S}$: C, 56.20; H, 4.72; N, 3.28. Found: C, 56.25; H, 4.68; N, 3.14.

2-(4-Methoxyphenyl)amino-2-trifluoromethyl-3-tosylmethyl-4-butanolide (2e).

Reaction of **1e** (139 mg, 0.30 mmol) with DIBAL-H (0.66 mmol) in THF gave **2e** (94 mg; 70% yield).

Colorless crystals: mp 163-164 °C (sublimation started at 154 °C); ^1H NMR (300 MHz, CDCl_3) δ 2.48 (s, 3H, *p*-tolyl CH_3), 3.16 (dd, 1H, $J = 14.4, 11.8$ Hz, CHCH(H)Ts), 3.45 (d, 1H, $J = 14.4$ Hz, CHCH(H)Ts), 3.70-3.75 (m, 1H, $\text{CH}_2\text{CHCH}_2\text{Ts}$), 3.77 (s, 3H, *p*-anisidyl OCH_3), 4.68 (dd, 1H, $J = 9.9, 5.8$ Hz, OCH(H)CH), 4.76 (d, 1H, $J = 9.6$ Hz, OCH(H)CH), 6.60 (d, 2H, $J = 8.9$ Hz, *p*-anisidyl H), 6.74 (dd, 2H, $J = 6.7, 2.1$ Hz, *p*-anisidyl H), 7.40 (d, 2H, $J = 8.2$ Hz, *p*-tolyl H), 7.76 (d, 2H, $J = 8.1$ Hz, *p*-tolyl H); IR (KBr) 3317, 1781, 1513, 1313, 1301, 1289, 1246, 1179, 1144, 1016, 556 cm^{-1} . Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{F}_3\text{NO}_5\text{S}$: C, 54.17; H, 4.55; N, 3.16. Found: C, 53.98; H, 4.64; N, 3.10.

2-Benzylamino-3, 4-dimethyl-2-trifluoromethyl-4-pentanolide (2f).

Reaction of **1f** (140 mg, 0.45 mmol) with DIBAL-H (0.99 mmol) in THF gave **2f** (103 mg; 79% yield).

A colorless oil: bp 132 °C/1.3 mmHg (short-path distillation); ^1H NMR (300 MHz, CDCl_3) δ 1.13 (d, 3H, $J = 6.9$ Hz, CH_3CHO), 1.46 (d, 3H, $J = 6.2$ Hz, CHCH_3), 1.70 (br s, 1H, NHCH_2Ph), 2.43 (dq, 1H, $J = 9.7, 6.8$ Hz, CHCHCH_3), 3.95-4.10 (br m, 2H, NHCH_2Ph), 4.41 (dq, 1H, $J = 9.7, 6.1$ Hz, CH_3CHO), 7.26-7.73 (m, 5H, phenyl H); IR (KBr) 3357, 1776, 1455, 1302, 1271, 1226, 1190, 1170, 1147, 1103, 999, 698 cm^{-1} ; LRMS (EI 70 eV) 287 (M^+ , 0.5), 286 ($\text{M}^+ - 1$, 1.2), 244 (0.6), 228 (2.5), 214 (17.6), 200 (1.2), 167 (8.4), 149 (1.2), 106 (100), 91 (88.8), 65 (8.4). Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{F}_3\text{NO}_2 + 0.4 \text{H}_2\text{O}$: C, 57.89; H, 5.83; N 4.82. Found: C, 57.92; H 5.79; N, 4.73.

2-(4-Methoxyphenyl)amino-3, 4-dimethyl-2-trifluoromethyl-4-pentanolide (2g).

Reaction of **1g** (133 mg, 0.41 mmol) with DIBAL-H (0.90 mmol) in THF gave **2g** (105 mg; 84% yield).

Colorless crystals: mp 87-88 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.25 (d, 3H, *J* = 6.9 Hz, CH₃CHO), 1.47 (d, 3H, *J* = 6.2 Hz, CHCH₃), 2.49 (dq, 1H, *J* = 9.6, 6.8 Hz, CHCHCH₃), 3.45 (br s, 1H, *p*-anisidyl NH), 3.77 (s, 3H, *p*-anisidyl OCH₃), 4.43 (dq, 1H, *J* = 9.6, 6.1 Hz, CH₃CHO), 6.78 (dd, 2H, *J* = 6.7, 2.3 Hz, *p*-anisidyl *H*), 6.93 (d, 2H, *J* = 8.9 Hz, *p*-anisidyl *H*); IR (KBr) 3330, 1774, 1512, 1303, 1248, 1194, 1144, 1032, 991, 831 cm⁻¹. Anal. Calcd for C₁₄H₁₆F₃NO₃: C, 55.45; H, 5.32; N, 4.62. Found: C, 55.43; H, 5.52; N, 4.51.

2-Benzylamino-2-trifluoromethyl-4-pentanolide (2h).

Reaction of **1h** (177 mg, 0.60 mmol) with DIBAL-H (1.3 mmol) in THF (25 h under reflux) gave **2h** (99.3 mg; 60% yield) along with the unchanged **1h** (7 mg; 4% yield).

A colorless oil: bp 133 °C/3.8 mmHg (short-path distillation); ¹H NMR (300 MHz, CDCl₃) δ 1.49 (d, 3H, *J* = 6.3 Hz, CH₃CHO), 2.07 (difused, 1H, NHCH₂Ph), 2.14 (dd, 1H, *J* = 13.9, 9.5 Hz, CHCH(H)C), 2.53 (dd, 1H, *J* = 13.7, 5.8 Hz, CHCH(H)C), 3.94 (br d, 2H, *J* = 7.6 Hz, NHCH₂Ph), 4.81 (ddq, 1H, *J* = 9.4, 6.2, 6.2 Hz, CH₃CHCH₂), 7.27-7.37 (m, 5H, phenyl *H*); IR (KBr) 3344, 2983, 1778, 1454, 1319, 1207, 1155, 1095, 982, 939, 731, 698 cm⁻¹. Anal. Calcd. for C₁₃H₁₄F₃NO₂: C, 57.14; H, 5.16; N, 5.13. Found: C, 57.33; H, 5.15; N, 5.09.

2-Benzylamino-6-methyl-2-trifluoromethyl-4-heptanolide (2i).

Reaction of **1i** (201 mg, 0.60 mmol) with DIBAL-H (1.3 mmol) in THF (48 h under reflux) gave **2i** (88 mg; 46% yield) along with the unchanged **1i** (34 mg; 16% yield).

A colorless oil: bp 148 °C/1.4 mmHg (short-path distillation); ¹H NMR (300 MHz, CDCl₃) δ 0.95

(t, 6H, $J = 6.3$ Hz, $(\text{CH}_3)_2\text{CH}$), 1.45 ((ddd, 1H, $J = 13.8, 7.7, 4.8$ Hz, $\text{CHCH}(H)\text{CH}$), 1.72 (td, 1H, $J = 6.0, 8.5$ Hz, $\text{CHCH}(H)\text{CH}$), 1.80 (octet, 1H, $J = 6.7$ Hz, $(\text{CH}_3)_2\text{CHCH}$), 2.08 (t like, 1H, $J = 6.0$ Hz, NHCH_2Ph), 2.12 (dd, 1H, $J = 13.8, 9.4$ Hz, $\text{CHCH}(H)\text{C}$), 2.48 (dd, 1H, $J = 13.5, 5.8$ Hz, $\text{CHCH}(H)\text{C}$), 3.92 (dd, 1H, $J = 13.0, 7.4$ Hz, $\text{NHCH}(H)\text{Ph}$), 3.96 (dd, 1H, $J = 13.3, 5.6$ Hz, $\text{NHCH}(H)\text{Ph}$), 7.27-7.36 (m, 5H, phenyl H), 4.70 (tt, 1H, $J = 9.4, 4.9$ Hz, CH_2CHCH_2); IR (KBr) 3347, 2959, 1779, 1469, 1455, 1286, 1202, 1169, 1106, 1016, 994, 698 cm^{-1} . Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{F}_3\text{NO}_2$: C, 60.94; H, 6.39; N, 4.44. Found: C, 60.98; H, 6.66; N, 4.38.

2-Benzylamino-2-trifluoromethyl-4-octanolide (**2j**).

Reaction of **1j** (170 mg, 0.51 mmol) with DIBAL-H (1.1 mmol) in THF gave **2j** (90 mg; 56% yield) along with the unreacted **1j** (9 mg; 5% yield).

A colorless oil: bp 160 °C/1.4 mmHg (short-path distillation); ^1H NMR (300 MHz, CDCl_3) δ 0.93 (t, 3H, $J = 6.9$ Hz, CH_3CH_2), 1.29-1.89 (m, 6H, $\text{CH}_3(\text{CH}_2)_3\text{CH}$), 2.06 (t, 2H, $J = 6.7$ Hz, NHCH_2Ph), 2.15 (dd, 1H, $J = 13.8, 9.5$ Hz, $\text{CHCH}(H)\text{C}$), 2.48 (dd, 1H, $J = 13.9, 5.9$ Hz, $\text{CHCH}(H)\text{C}$), 3.92 (dd, 1H, $J = 13.0, 7.4$ Hz, $\text{NHCH}(H)\text{Ph}$), 3.96 (dd, 1H, $J = 12.9, 5.8$ Hz, $\text{NHCH}(H)\text{Ph}$), 4.64 (ddt, 1H, $J = 9.5, 7.5, 5.6$ Hz, CH_2CHCH_2), 7.36-7.27 (m, 5H, phenyl H); IR (KBr) 3347, 2958, 2935, 2872, 1778, 1455, 1282, 1200, 1169, 1106, 993, 698 cm^{-1} . Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{F}_3\text{NO}_2$: C, 60.94; H, 6.39; N, 4.40. Found: C, 60.84; H, 6.45; N, 4.41.

(3*S*)-(E)-3-Hydroxy-1-tosyl-1-butene [(3*S*)-**9**].

The kinetic resolution of (*E*)-3-hydroxy-1-butene (**9**) was performed according to the literatures.¹⁰

To a mixture of racemic (*E*)-3-hydroxy-1-tosyl-1-butene[(*rac*)-**9**] (906 mg, 4.0 mmol) and well-ground molecular sieves (MS4A, 910 mg) in benzene (14 mL), vinyl acetate (1.85 mL, 20 mmol) and Lipase PS (2.00 g) were added. After being stirred for 5 h at room temperature, the reaction mixture was filtered by a celite column. The filtrate was concentrated in vacuo and

chromatographed on silica gel [eluent: *n*-hexane-ethyl acetate (2 : 1)] to give (3*S*)-**9** (442 mg; 49% yield).

Colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 1.36 (d, 3H, *J* = 6.7 Hz, CH₃CH), 1.68 (d, 1H, *J* = 4.8 Hz, CHOH), 2.45 (s, 3H, *p*-tolyl CH₃), 4.54 (m, 1H, CH₃CHCH), 6.58 (dd, 1H, *J* = 15.0, 1.8 Hz, CHCH=CHTs), 6.96 (dd, 1H, *J* = 14.8, 3.7 Hz, CHCH=CHTs), 7.34 (d, 2H, *J* = 8.0 Hz, *p*-tolyl *H*), 7.77 (d, 2H, *J* = 8.2 Hz, *p*-tolyl *H*); IR (KBr) 3447, 3416, 1295, 1285, 1269, 1132, 1082, 1035, 840, 811, 666, 539, 516 cm⁻¹; [α]_D²⁵ 37 ° (*c* 0.10, CHCl₃); enantio excess: 98%ee [Chiral HPLC: Chiralcel OD, eluent: *n*-hexane-*iso*-PrOH (15 : 1), 0.7 mL/min, *t*_R = 40.1 min. *cf.* (3*R*)-**9** *t*_R = 49.1 min].

(2*R*, 3*S*, 4*S*)-2-fluoro-4-methyl-3-tosylmethyl-2-trifluoromethyl-4-pentanolide [(2*R*,3*S*,4*S*)-3I**].**

To a solution of (3*S*)-**9** (200 mg, 0.88 mmol) in chloroform (4.4 mL), a solution of hexafluoropropene-diethylamine adduct (PPDA) (1.19 mL, 1.1 mmol) in chloroform (1.2 mL) was dropwise added over 8 min at room temperature. After being stirring for 2 h at the same temperature, the reaction was quenched with water (10 mL). The resulting mixture was extracted with chloroform (3 × 10 mL). The organic layers were washed with brine (3 × 10 mL), dried over MgSO₄, and concentrated in vacuo. The residue was chromatographed on silica gel [eluent: *n*-hexane-ethyl acetate (3 : 1)] to give a colorless oil (336 mg) which contained (2*R*,3*S*,4*S*)-**3I** and **9**. The further purification of this oil was performed by GPC [eluent: chloroform] afforded (2*R*,3*S*,4*S*)-**3I** (233 mg; 74% yield).

Colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 1.73 (d, 3H, *J* = 6.2 Hz, CH₃CH), 2.49 (s, 3H, *p*-tolyl CH₃), 3.15-3.30 (m, 2H, *J* = 12.8 Hz, FCCHCH₂Ts and CHCH(*H*)Ts), 3.55 (d like, 1H, *J* = 10.3 Hz, CHCH(*H*)Ts), 4.67 (quintet like, 1H, *J* = 6.6 Hz, CH₃CHCH), 7.42 (d, 2H, *J* = 8.6 Hz, *p*-tolyl *H*), 7.82 (d, 2H, *J* = 8.4 Hz, *p*-tolyl *H*); IR (KBr) 1803, 1326, 1289, 1253, 1207, 1173, 1153, 1087, 1057, 1023, 814, 751 cm⁻¹; [α]_D¹⁹ 9.0 ° (*c* 1.0, CHCl₃); enantio excess: > 99%ee [Chiral

HPLC: Chiralcel OD, eluent: *n*-hexane-*iso*-PrOH (15 : 1), 0.7 mL/min, $t_R = 22.4$ min. *cf.* (2*S*,3*R*,4*R*)-**3l** $t_R = 26.4$ min].

Preparation of (2*R*,3*S*,4*S*)-*N*-Benzyl-4-hydroxy-2-fluoro-3-tosylmethyl-2-(trifluoromethyl)-pentanamide [(2*R*,3*S*,4*S*)-1b**].**

According to the same procedure described for **1b**, (2*R*,3*S*,4*S*)-**1b** was prepared from (2*R*,3*S*,4*S*)-**3l**.

Its ^1H NMR and IR data were identical to those of racemic **1b**. $[\alpha]_D^{25} -8.3^\circ$ (*c* 0.11, CHCl_3); Enantio excess: > 99%ee [Chiral HPLC: Chiralcel OD, eluent: *n*-hexane : *iso*-PrOH (15 : 1), 0.7ml/min, $t_R = 37.3$ min. *cf.* (2*S*,3*R*,4*R*)-**1b** $t_R = 31.4$ min];.

Preparation of (2*S*,3*S*,4*S*)-2-Benzylamino-2-trifluoromethyl-3-tosylmethyl-4-pentanolide [(2*S*,3*S*,4*S*)-2b**].**

According to the same procedure described for **2b**, (2*S*,3*S*,4*S*)-**2b** was prepared from (2*R*,3*S*,4*S*)-**1b**. A pure sample of (2*S*,3*S*,4*S*)-**2b** was obtained by recrystallization from *n*-hexane-chloroform.

The spectroscopic properties (^1H NMR, IR) were identical to racemic **2b**. $[\alpha]_D^{25} -81^\circ$ (*c* 0.11, CHCl_3); Enantio excess: > 99%ee [Chiral HPLC: Chiralcel OD, eluent: *n*-hexane : *iso*-PrOH (4 : 1), 0.7 mL/min, $t_R = 21.7$ min. *cf.* (2*S*,3*S*,4*S*)-**2b** $t_R = 58.3$ min].

1f

19

11

1j

10h

10i

10j

2f

29

2h

2i

2j

5b

(* : Ethyl acetate)

8

(S)-9

(2*R*,3*S*,4*S*)-**31**

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