

Enantioselective Fluorination of Organic Molecules. I. Synthetic Studies of the Agents for Electrophilic, Enantioselective Fluorination of Carbanions

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In order to develop novel methods for electrophilic and enantioselective fluorination of active methine compounds, preliminary experiments were carried out. The *N*-tosyl derivative **5** obtained from *D*-phenylglycine was fluorinated with FCIO_3 or diluted F_2 gas to give the *N*-fluoro-*N*-tosyl derivative **6**. *N*-Tosyl- or *N*-mesyl-(*S*)- α -phenethylamine **7** or **8** was subjected to FCIO_3 fluorination to produce the corresponding *N*-fluoro derivative, **10** or **11**, respectively. Enantioselective fluorination of some methine compounds was attempted employing the above *N*-fluoro agents. Best result was obtained when 2-benzyl-1-tetralone/KHMDS was treated with **10** to produce the fluorinated tetralone **17** in 53% yield with enantiomeric excess (ee) of 48%.

Key words fluorinating agent; electrophilic fluorination; enantioselective fluorination; FCIO_3 ; *N*-fluorosulfonamide derivative

The replacement of a carbon–hydrogen bond with a carbon–fluorine bond continues to be an effective approach to the development of analogs of biologically active compounds as potential medicinal and pharmacological agents.¹⁾ The stereoselective preparation of chiral monofluoro compounds is an important goal with respect to the development of fluorinated synthetic building blocks as well as target bioactive molecules. Several methods have been reported for the diastereoselective fluorination of enolates that have chiral auxiliaries in the substrates.²⁾ However, relatively few methods have been reported that employ stereoselective fluorinating agents where the asymmetry-inducing factor is resident in the agents themselves. Two groups have described³⁾ new *N*-fluorosultams **1** and **2**, and reported maximum enantiomeric excess (ee) values of 70% and 75% for **1** and **2**, respectively, for the fluorination of enolates. Unfortunately, structural modifications of **1** and **2** to produce more efficient agents with respect to chemical and optical yields may be difficult because these sultams originate from natural products.

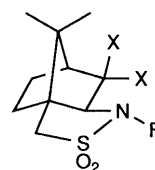
We have begun research directed toward developing new enantioselective fluorinating agents based on the use of readily available chiral amines as starting materials. In our approach, initial lead compounds will be amenable to ready structural modifications in order to provide information that will facilitate development of stable *N*-fluoro compounds that are capable of efficient enantioselective fluorination. We present here our preliminary results on the synthesis of *N*-fluoro compounds designed to this end.

Based on the structural factors discussed above, we first focused on amino acid derivatives. *N*-Tosyl- or *N*-mesyl-*D*-phenylglycine ethyl ester **3** in tetrahydrofuran (THF) was treated with NaH and subjected to our mild fluorination with FCIO_3 ⁴⁾ at 0 °C. However, no fluorine-containing compounds could be isolated under these conditions. Using stronger fluorination condition, 15% F_2 -He gas was introduced into a solution of **3** (R = Ts, Ms) in

$\text{CFCl}_3/\text{CHCl}_3$ at –40 °C, to afford ethyl benzoylformate (**4**) as an only isolable product. This can be explained by facile dehydrofluorination of initially formed *N*-fluoro product to give the imine, which was hydrolyzed during workup to give **4**, as shown in Chart 1.

In order to suppress dehydrofluorination, we considered manipulation of the ester moiety to reduce the acidity of the α -proton. Thus, the ester **3** (R = Ts) was reduced with LiAlH_4 to give (*R*)-phenylglycinol, which was acetylated with $\text{Ac}_2\text{O}/\text{Pyr}$ to afford the acetate **5** in good yield. Mild fluorination of **5** with FCIO_3/NaH at 0 °C resulted in isolation of the target molecule **6** in approximately 27% yield, along with unreacted starting material. On the other hand, use of 15% F_2 -He/spray-dried KF⁵⁾ in $\text{CFCl}_3/\text{CHCl}_3$ at –78 °C gave **6** in less than 10% yield accompanied by apparent overfluorination or oxidation.

We next considered α -phenethylamine as starting material, considering that this molecule is further deactivated with respect to dehydrofluorination, and also is readily available in optically active form. Fluorination of *N*-tosyl-, *N*-mesyl-, or *N*-trifluoromethanesulfonyl (triflyl, Tf)-(*S*)- α -phenethylamine (**7**, **8**, or **9**) was attempted employing 15% F_2 -He/spray-dried KF as described above, to produce a mixture of several products. Fluorination of **7** and **8** using the milder FCIO_3/NaH procedure afforded the *N*-fluoro derivatives **10** and **11**, respectively, albeit in modest yields. Fluorination of **9** under these conditions led to extensive decomposition, apparently due to the instability of the corresponding *N*-fluoro derivative.⁶⁾ In this series, the



1 : X = H

2 : X = Cl

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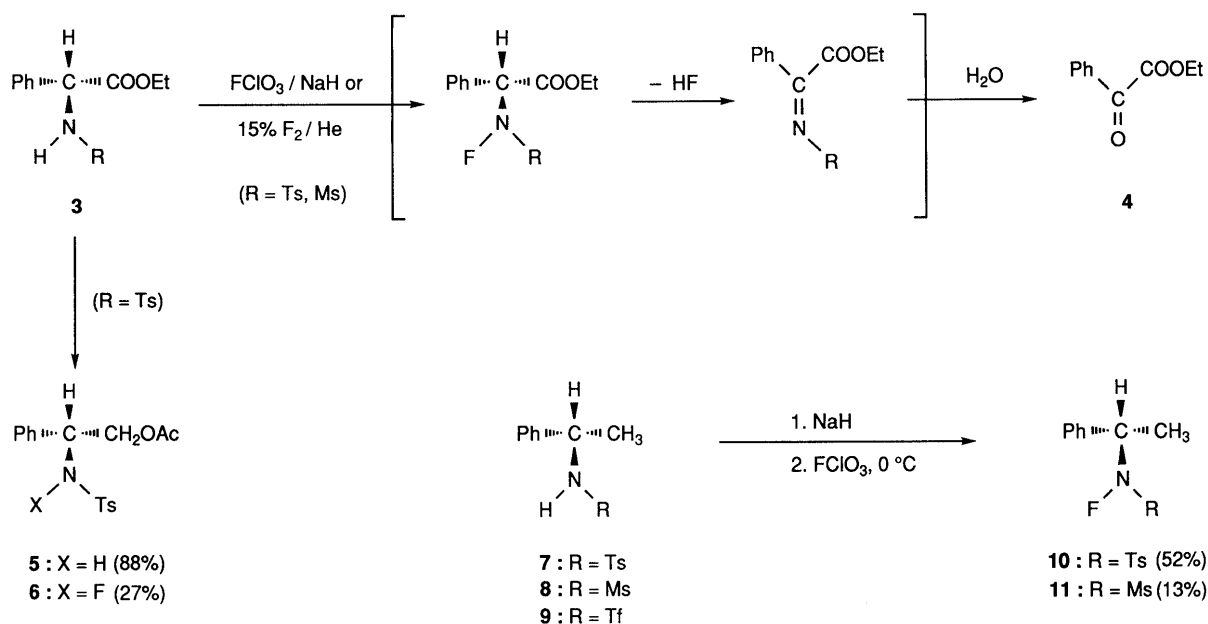


Chart 1

tassel derivative **10** was found to be the most stable, so we next examined varying conditions for the FClO_3 fluorination of **7** in order to optimize the formation of **10**. Several bases were examined, including lithium diisopropylamide (LDA), BuLi, NaH, and KH, in combination with various solvents, including THF, dimethylformamide (DMF), ether, and THF/hexamethylphosphoramide (HMPA) at temperature ranging from -78°C to room temperature. The best result was obtained when **7** was treated with NaH and allowed to react with FClO_3 at 0°C for 3 h. Under these optimized conditions, the *N*-fluoro derivative **10** was isolated in 52% yield, after purification by silica gel chromatography (Chart 1).

Having been in hand the *N*-fluoro derivatives **6**, **10**, and **11**, we now turned to examine the potential of this class of chiral reagent for enantioselective electrophilic fluorination, using 2-methyl-1-tetralone (**12**) as a model compound. A solution of **12** in THF was treated with an appropriate base at -40°C and then allowed to react with the *N*-fluoro compound at -40 – 0°C for 3 h. After usual workup, the product **13**³¹ was isolated by silica gel chromatography and the ee was determined by HPLC using a chiralcel OB⁷¹ column. Unfortunately, in all experiment both chemical and optical yields were disappointing (Table 1).

We carried out similar fluorinations using other substrates, including 2-benzyl-1-tetralone (**14**), ethyl 2-oxocyclopentanecarboxylate (**15**), and ethyl 2-benzoylpropionate (**16**), with 1.1 eq of **6**, **10**, or **11** in THF. The corresponding monofluoro compounds **17**, **18**,³¹ and **19** were isolated and analyzed as before (Table 2). Again, low chemical and optical yields were obtained.

Our initial experiments have not produced practical fluorinating agents, although we have gained insight into requirements for reagent preparation and subsequent fluorinations. The low chemical yields in the fluorinations presumably reflect low reactivities of these *N*-fluoro compounds. Whereas additional studies to define more

Table 1. Enantioselective Fluorination of 2-Methyl-1-tetralone with the *N*-F Derivative **6**, **10**, or **11**

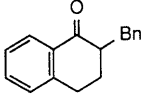
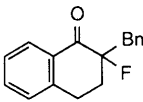
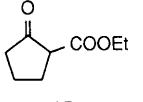
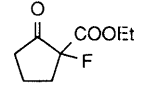
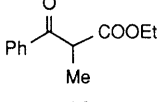
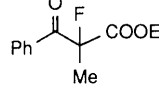
Run	Fluorinating reagent	Base	ee (yield), %
1	6 (1.1 eq)	LDA	2 (12)
2	6 (1.1 eq)	KHMDS	8 (8)
3	10 (1.1 eq)	LDA	46 (16)
4	10 (2.0 eq)	LDA	32 (37)
5	10 (1.1 eq)	NaH	— (0)
6	10 (1.1 eq)	KH	— (0)
7	10 (1.1 eq)	KHMDS	46 (46)
8	10 (1.1 eq)	LHMDS	46 (3)
9	10 (1.1 eq)	NaHMDS	32 (16)
10	11 (0.9 eq)	LDA	20 (11)

precisely optimal reaction conditions for fluorination may be appropriate, the low ee values suggest that further structural modifications of the reagents are required. These low ee values also have discouraged us from determining the absolute configuration of the products. Included in plans for future work are synthesis of cyclic *N*-fluoro-sulfonamides that should be more effective in controlling transition state geometry and, thus, increasing enantioselection.

Experimental

General Notes Melting points were determined on a Yanagimoto micro-melting point apparatus and uncorrected. IR spectra were recorded on a Perkin-Elmer 1600 spectrometer. ^1H -NMR spectra were measured with Me_4Si as an internal standard and were recorded on a JEOL GX-270 (270 MHz) or a Varian Gemini 300 (300 MHz) spectrometer. ^{19}F -NMR spectra were measured with CFCl_3 as an internal standard and were taken with a JEOL GX-270 (254 MHz) spectrometer. Upfield shifts are quoted as negative δ values. EI mass spectra were taken with a JEOL JMS-D300 spectrometer. Column chromatography and preparative TLC

Table 2. Enantioselective Fluorination of Some Active Methine Compounds with the N-F Derivative **6**, **10**, or **11**

$ \begin{array}{ccc} \text{R}^1 & & \text{R}^2 \\ & \text{O} & \\ & \parallel & \\ & \text{C} & \\ & & \\ & \text{R}^3 & \\ \text{14--16} & \xrightarrow[\text{THF}]{\text{6, 10, or 11}} & \text{17--19} \end{array} $					
Entry	Starting material	Fluorinating reagent	Conditions (base, temp.)	Product	ee (yield), %
1	 14	6 (1.1 eq)	LDA, -40—-20 °C	 17	9 (6)
2		10 (1.1 eq)	LDA, -40—-20 °C		54 (26)
3		10 (1.1 eq)	KHMDS, -40—-20 °C		48 (53)
4		11 (1.1 eq)	LDA, -40—-20 °C		6 (8)
5	 15	6 (1.1 eq)	NaH, 0 °C	 18	6 (23)
6		10 (1.1 eq)	NaH, 0 °C—r.t.		14 (20)
7		11 (1.1 eq)	NaH, 0 °C		30 (6)
8	 16	6 (1.1 eq)	NaH, 0 °C	 19	8 (4)
9		10 (1.1 eq)	NaH, 0 °C		18 (21)
10		11 (1.1 eq)	NaH, 0 °C		6 (21)

were performed on BW-200 (Fuji Silysia) and Kieselgel 60 (Merck, art. 7748), respectively.

Preparation of *N*-(*R*)-(2-Acetoxy-1-phenylethyl)-*p*-toluenesulfonamide (5**)** To a stirred solution of *N*-*p*-toluenesulfonyl-(*R*)-phenylglycine ethyl ester (3.33 g, 10 mmol) in THF (100 ml) under N₂ at 0 °C was added LiAlH₄ (569 mg, 15 mmol) and the mixture was stirred at 0 °C for 30 min. To the mixture was successively added EtOH (10 ml), water (10 ml) and 10% HCl (10 ml) and the whole was concentrated to one third of the original volume. The residue was extracted with AcOEt (50 ml × 3) and the extract was dried on MgSO₄. Evaporation of the solvent gave an oil, which was chromatographed on silica gel (hexane:AcOEt = 1:1) to give 2.91 g (100%) of the corresponding phenylglycinol as colorless prisms. mp 105 °C.

To a solution of the phenylglycinol (70 mg, 0.24 mmol) and pyridine (0.02 ml, 0.24 mmol) in ether (8 ml) was added Ac₂O (0.023 ml, 0.24 mmol) and the solution was stirred at room temperature for 40 h. The resulting solution was washed with water (5 ml × 3) and dried on MgSO₄. Evaporation of the solvent gave a yellow oil, which was chromatographed on silica gel (hexane:AcOEt = 2:1) to give 70.4 mg (88%) of **5**. Colorless prisms. mp 78 °C. IR (KBr): 3237 (NH), 1740 (CO), 1325 and 1157 (SO₂) cm⁻¹. ¹H-NMR (CDCl₃) δ: 1.94 (3H, s, OCOCH₃), 2.37 (3H, s, *p*-CH₃-Ph), 4.17 (2H, m, CH₂), 4.62 (1H, dd, *J* = 7.1, 5.0 Hz, CH), 5.38 (1H, brs, NH), 7.13—7.61 (9H, m, Ph). MS *m/z*: 333 (M⁺), 274 (M⁺ - OAc), 260 (M⁺ - CH₃OAc), 155 (Ts⁺), 91 (*p*-CH₃-Ph⁺).

Preparation of *N*-(*R*)-(2-Acetoxy-1-phenylethyl)-*N*-fluoro-*p*-toluenesulfonamide (6**)** A solution of **5** (1.2 g, 3.6 mmol) in THF (180 ml) was treated with NaH (60% dispersion in mineral oil, 260 mg, 6.5 mmol) under N₂ at 0 °C and the mixture was stirred at 0 °C for 1 h. To the mixture was introduced freshly generated FClO₃ gas⁴ at 0 °C for 2 h. Insoluble materials were removed by filtration and concentration of the filtrate gave an oil, which was chromatographed on silica gel (hexane:AcOEt = 3:1) to give 340 mg (27%) of **6**. Colorless prisms. mp 60—61 °C. IR (KBr): 1740 (COO), 1369 and 1171 (SO₂) cm⁻¹. ¹H-NMR (CDCl₃) δ: 2.04 (3H, s, OCOCH₃), 2.41 (3H, s, *p*-CH₃-Ph), 4.37—4.70 (2H, m, CH₂), 5.16 (1H, ddt, *J* = 36.5, 5.6, 2.1 Hz, CH), 7.21—7.69 (9H, m, Ph). ¹⁹F-NMR (CDCl₃) δ: -72.1 (d, *J* = 36.7 Hz, NF). MS *m/z*: 332 (M⁺ - F), 331 (M⁺ - HF), 278 (M⁺ - CH₂OAc), 260 (M⁺ - *p*-CH₃-Ph). Anal. Calcd for C₁₇H₁₈FNO₄S: C, 58.12; H, 5.13; N, 3.99. Found: C, 58.30; H, 5.05; N, 3.64.

General Procedure for Preparation of Sulfonamide Derivatives **7, **8** and **9**** To a stirred solution of (*S*)-α-phenethylamine (15.6 ml, 121 mmol) and triethylamine (33 ml, 240 mmol) in benzene or THF (300 ml) at 0 °C was added *p*-toluenesulfonyl chloride, methanesulfonyl chloride, or trifluoromethanesulfonyl chloride (130 mmol) in benzene or THF (200 ml) and the mixture was stirred at room temperature for 12—15 h.

The mixture was filtered and the filtrate was washed with water (100 ml × 3) and dried on MgSO₄. Evaporation of the solvent gave a residue, which was recrystallized or chromatographed on silica gel to give **7** (29.6 g, 89%), **8** (22.4 g, 93%), or **9** (10.7 g, 35%), respectively.

***N*-(*S*)-(1-Phenylethyl)-*p*-toluenesulfonamide (**7**)** Colorless prisms. mp 99.0—99.5 °C. [α]_D²⁴ -65.32° (*c* = 0.99, CHCl₃). IR (KBr): 3252 (NH), 2972, 1319 and 1162 (SO₂) cm⁻¹. ¹H-NMR (CDCl₃) δ: 1.43 (3H, d, *J* = 6.9 Hz, CH₃), 2.39 (3H, s, *p*-CH₃-Ph), 4.46 (1H, q, *J* = 6.7 Hz, CH), 4.74 (1H, brs, NH), 7.08—7.64 (9H, m, Ph). MS *m/z*: 275 (M⁺), 260 (M⁺ - CH₃), 155 (Ts⁺), 120 (M⁺ - Ts), 105 (M⁺ - NHTs), 91 (*p*-CH₃-Ph⁺), 77 (Ph⁺). Anal. Calcd for C₁₅H₁₇NO₂S: C, 65.43; H, 6.22; N, 5.09. Found: C, 65.49; H, 6.18; N, 5.27.

***N*-(*S*)-(1-Phenylethyl)methanesulfonamide (**8**)** Colorless prisms. mp 54.0—55.0 °C. IR (KBr): 3289 (NH), 1319 and 1150 (SO₂) cm⁻¹. ¹H-NMR (CDCl₃) δ: 1.55 (3H, d, *J* = 6.9 Hz, CH₃), 2.62 (3H, s, SO₂CH₃), 4.65 (1H, dq, *J* = 6.9 Hz, CH), 4.83 (1H, d, *J* = 6.9 Hz, NH), 7.34 (5H, m, Ph). MS *m/z*: 199 (M⁺), 184 (M⁺ - CH₃), 105 (M⁺ - NHMs). Anal. Calcd for C₉H₁₃NO₂S: C, 54.25; H, 6.58; N, 7.03. Found: C, 54.00; H, 6.42; N, 6.95.

***N*-(*S*)-(1-Phenylethyl)trifluoromethanesulfonamide (**9**)** Pale yellow oil. IR (neat): 3309 (NH), 1372 and 1195 (SO₂) cm⁻¹. ¹H-NMR (CDCl₃) δ: 1.64 (3H, d, *J* = 6.8 Hz, CH₃), 4.80 (1H, q, *J* = 6.8 Hz, CH), 5.31 (1H, brs, NH), 7.34 (5H, m, Ph). ¹⁹F-NMR (CDCl₃) δ: -78.1 (s, CF₃). MS *m/z*: 253 (M⁺), 238 (M⁺ - CH₃), 105 (M⁺ - NHTf).

General Procedure for Fluorination of Sulfonamide Derivatives **7 and **8**** A solution of **7** or **8** (7.27 mmol) in THF (300 ml) was treated with NaH (60% dispersion in mineral oil, 500 mg, 12.5 mmol) under N₂ at 0 °C and the mixture was stirred at 0 °C for 1 h. To the mixture was introduced freshly generated FClO₃ gas⁴ at 0 °C for 3 h. Insoluble materials were removed by filtration and concentration of the filtrate gave a residue, which was chromatographed on silica gel to give **10** (1.1 g, 52%) or **11** (205 mg, 13%), respectively.

***N*-Fluoro-*N*-(*S*)-(1-phenylethyl)-*p*-toluenesulfonamide (**10**)** Colorless prisms. mp 64.0—64.5 °C. [α]_D²⁴ -10.28° (*c* = 1.03, CHCl₃). IR (KBr): 2996 (CH₃), 1371 and 1173 (SO₂) cm⁻¹. ¹H-NMR (CDCl₃) δ: 1.65 (3H, dd, *J* = 6.8, 1.2 Hz, CH₃), 2.44 (3H, s, *p*-CH₃-Ph), 4.92 (1H, dq, *J* = 32.5, 6.8 Hz, CH), 7.19—7.80 (9H, m, Ph). ¹⁹F-NMR (CDCl₃) δ: -66.5 (d, *J* = 31.3 Hz, NF). MS *m/z*: 293 (M⁺), 274 (M⁺ - F), 155 (Ts⁺), 91 (*p*-CH₃-Ph⁺). Anal. Calcd for C₁₅H₁₆FNO₂S: C, 61.42; H, 5.50; N, 4.77. Found: C, 61.57; H, 5.57; N, 4.80.

***N*-Fluoro-*N*-(*S*)-(1-phenylethyl)methanesulfonamide (**11**)** Pale yellow oil. IR (neat): 1356 and 1169 (SO₂) cm⁻¹. ¹H-NMR (CDCl₃) δ: 1.76 (3H, d, *J* = 6.8 Hz, CH₃), 2.90 (3H, s, SO₂CH₃), 5.10 (2H, dq, *J* = 38.8, 6.9 Hz, CH), 7.33—7.41 (5H, m, Ph). ¹⁹F-NMR (CDCl₃) δ: -73.2 (d, *J* = 38.6 Hz, NF). MS *m/z*: 217 (M⁺), 197 (M⁺ - HF), 105 (M⁺ - NF

—Ms).

General Procedure for Enantioselective Fluorination of Active Methine Compounds A solution of **12**, **14**, **15**, or **16** (0.25 mmol) in THF (2.5 ml) was treated with an appropriate base (0.3 mmol) under N₂ at -78 – 0 °C and the mixture was stirred at -40 – 0 °C for 30 min. To the mixture was added **6**, **10**, or **11** (0.28 mmol) in THF (0.5 ml) at -40 – 0 °C and the whole mixture was stirred for 3 h. Reaction was quenched by adding saturated NH₄Cl (2 ml). The mixture was extracted with AcOEt (10 ml $\times$ 3) and the extract was dried on MgSO₄. Evaporation of the solvent gave an oil, which was purified by silica gel preparative TLC to give **13**, **17**, **18**, or **19** (Tables 1 and 2).

2-Fluoro-2-methyl-1-tetralone (13)³⁾ Colorless oil. IR (neat): 2938 (CH₂), 1701 (CO) cm⁻¹. ¹H-NMR (CDCl₃) δ : 1.60 (3H, d, J =22.2 Hz, CH₃), 2.21–2.57 (2H, m, Ar-CH₂-CH₂), 2.95–3.23 (2H, m, Ar-CH₂-CH₂), 7.25–8.09 (4H, m, Ph). ¹⁹F-NMR (CDCl₃) δ : -155.1 (qdd, J =22.1, 16.6, 9.2 Hz). MS m/z : 178 (M⁺). Ee value of **13** was determined by HPLC using chiralcel OB⁷⁾ column (Daicel Chemical Co., hexane:2-PrOH=9:1). The major isomer was eluted prior to the minor isomer except for the case shown in run 10 (Table 1).

2-Benzyl-2-fluoro-1-tetralone (17) Colorless oil. IR (neat): 2927 (CH₂), 1698 (CO) cm⁻¹. ¹H-NMR (CDCl₃) δ : 2.04–2.35 (2H, m, Ar-CH₂-CH₂), 2.96–3.14 (3H, m, Ar-CH₂-CH₂, CH₄H_b), 3.32 (1H, dd, J =17.3, 14.9 Hz, CH₄H_b), 7.26–7.57 (7H, m, Ph), 8.10 (1H, d, J =7.8 Hz, Ph). ¹⁹F-NMR (CDCl₃) δ : -158.0 (dddd, J =31.3, 16.6, 16.5, 5.5 Hz). MS m/z : 254 (M⁺), 235 (M⁺-F), 163 (M⁺-Bn). Ee value of **17** was determined by HPLC using chiralcel OJ⁸⁾ column (Daicel Chemical Co., hexane:2-PrOH=9:1). The major isomer was eluted prior to the minor isomer (Table 2).

Ethyl 1-Fluoro-2-oxocyclopentanecarboxylate (18)³⁾ Colorless oil. IR (neat): 1771 (COO), 1729 (CO) cm⁻¹. ¹H-NMR (CDCl₃) δ : 1.32 (3H, t, J =7.1 Hz, CH₂CH₃), 2.08–2.64 (6H, m, CH₂), 4.29 (2H, q, J =7.1 Hz, CH₂CH₃). ¹⁹F-NMR (CDCl₃) δ : -164.6 (t, J =20.2 Hz). MS m/z : 175 (M⁺+1), 174 (M⁺), 101 (M⁺-COOEt). Ee value of **18** was determined by HPLC using chiralcel OB⁷⁾ column (hexane:2-PrOH=9:1). The major isomer was eluted prior to the minor isomer (Table 2).

Ethyl 2-Benzoyl-2-fluoropropionate (19) Colorless oil. IR (neat): 1760 (COO), 1700 (CO) cm⁻¹. ¹H-NMR (CDCl₃) δ : 1.20 (3H, t, J =7.1 Hz, CH₂CH₃), 1.87 (3H, d, J =22.7 Hz, CH₃), 4.26 (2H, qd, J =7.1, 1.7 Hz, CH₂CH₃), 7.48 (2H, d, J =7.8 Hz, Ph), 7.43–7.62 (1H, m, Ph), 8.05

(2H, d, J =8.3 Hz, Ph). ¹⁹F-NMR (CDCl₃) δ : -152.3 (q, J =22.0 Hz). MS m/z : 224 (M⁺), 151 (M⁺-COOEt), 105 (PhCO⁺). Ee value of **19** was determined by HPLC using chiralcel OJ⁸⁾ column (hexane:2-PrOH=20:1). The major isomer was eluted prior to the minor isomer (Table 2).

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References

- 1) Filler R. (ed.), "Biochemistry Involving Carbon-Fluorine Bonds," American Chemical Society, Washington, DC, 1976; Filler R., Kobayashi Y. (eds.), "Biomedical Aspects of Fluorine Chemistry," Kodansha, Tokyo, 1982; Kirk K. L. (ed.), "Biochemistry of Halogenated Organic Compounds," Plenum, New York, 1991; Welch J. T., *Tetrahedron*, **43**, 3123 (1987).
- 2) Davis F. A., Han W., *Tetrahedron Lett.*, **33**, 1153 (1992); Siddiqui M. A., Marquez V. E., Driscoll J. S., Barchi J. J., Jr., *ibid.*, **35**, 3263 (1994); Ihara M., Kai T., Taniguchi N., Fukumoto K., *J. Chem. Soc., Perkin Trans. 1*, **1990**, 2357; Iwaoka T., Murohashi T., Sato M., Kaneko C., *Tetrahedron Asymmetry*, **8**, 1025 (1990).
- 3) Differding E., Lang R. W., *Tetrahedron Lett.*, **29**, 6087 (1988); Davis F. A., Zhou P., Murphy C. K., *ibid.*, **34**, 3971 (1993).
- 4) Takeuchi Y., Murayama A., Hagi T., Koizumi T., *J. Chem. Soc. Jpn.*, **1985**, 2029.
- 5) Ishikawa N., Kitazume T., Yamazaki T., Mochida Y., Tatsuno T., *Chem. Lett.*, **1981**, 761.
- 6) Bozec-Ogor S., Salou-Guizieu V., Yaouanc J. J., Handel H., *Tetrahedron Lett.*, **36**, 6063 (1995).
- 7) Okamoto Y., Kawashima M., Yamamoto K., Hatada K., *Chem. Lett.*, **1984**, 739; Ichida A., Shibata T., Okamoto I., Yuki Y., Namikoshi H., Toga Y., *Chromatographia*, **19**, 280 (1984); Shibata T., Okamoto I., Ishii K., *J. Liq. Chromatogr.*, **9**, 313 (1986).
- 8) Okamoto Y., Aburatani R., Hatada K., *J. Chromatogr.*, **389**, 95 (1987); Soons P. A., Rosemalen M. C. M., Breimer D. D., *ibid.*, **528**, 343 (1990); Eto S., Noda H., Noda A., *ibid.*, **568**, 157 (1991).