Supporting Information

Catalytic Enantioselective Fluorination of Oxindoles

Yoshitaka Hamashima,^a Toshiaki Suzuki,^a Hisashi Takano,^a Yuta Shimura,^a and Mikiko Sodeoka^{a,b,c*}

^a *Institute of Multidisciplinary Research for Advanced Materials, Tohoku University, Miyagi, 980-8577, Japan*

^b *PRESTO, Japan Science and Technology Agency (JST)*

^c *RIKEN, Hirosawa, Wako 351-0198, Japan*

General: NMR spectra were recorded on a JEOL JNM-LA400 spectrometer, operating at 400 MHz for ¹H-NMR, 100 MHz for ¹³C-NMR. Chemical shifts were reported downfield from TMS (= 0) for ¹H-NMR. For ¹³C-NMR, chemical shifts were reported in the scale relative to the solvent used as an internal reference. ¹⁹F-NMR was measured at 376 MHz, and CF₃COOH (TFA) was used as an external standard. FAB-LRMS was taken on JEOL JMS GCmate II or JEOL HX110 using *m*-nitrobenzyl alcohol (*m*NBA) as matrix. FAB-HRMS was also taken on JEOL JMS GCmate II or JEOL HX110 using *m*NBA as matrix and with PEG 400 as an internal standard. IR was measured on Thermo Nicolet AVATAR 370 FT-IR. Optical rotations were measured on a JASCO DIP-370 polarimeter. Column chromatography was performed with silica gel 60 (40-100 μm) purchased from KANTO CHEMICAL Co., INC. The enantiomeric excesses (ees) were determined by chiral HPLC analysis. HPLC analysis was performed on Shimadzu HPLC systems consisting of the followings: pump, LC-10AD; detector, SPD-10A measured at 254 nm. Also, JASCO HPLC systems were used consisting of the followings: pump, PU-2080 Plus; detector, CD-2095 Plus measured at 254 nm; column, DAICEL CHIRALPAK AD-H, AS-H, or DAICEL CHIRALCEL OD-H, OJ-H; mobile phase, hexane / 2-propanol (IPA). Dehydrated stabilizer-free tetrahydrofuran (THF) was purchased from KANTO CHEMICAL Co., INC. and was directly used without further purification. MeOH, EtOH, and *i*PrOH were distilled from calcium hydride. Other reagents were purified by usual methods.

1) Preparation of palladium complexes 1 and 2

The palladium aqua complexes **1** and palladium μ -hydroxo complexes **2** were prepared according to the reported procedures.¹

¹ (a) Fujii, A.; Hagiwara, E.; Sodeoka, M. *J. Am. Chem. Soc.* **1999**, *121*, 5450-5458. (b) Hamashima, Y.; Yagi, K.; Takano, H.; Tamás, L.; Sodeoka, M. *J. Am. Chem. Soc.* **2002**, *124*, 14530-14531.

2) Synthesis of *N*-protected oxindoles

2-1) Procedure for the synthesis of *N*-Boc-protected oxindoles **5b-c**, **5f-m**.

When the conventional methods² were employed, preparation of the starting materials examined in this paper was not successful. As shown in Scheme SI-1, the selective protection of the nitrogen moiety of the 3-substituted oxindoles with (Boc)₂O was difficult and accompanied *O*-protection to give a considerable amount of *N,O*-diBoc-protected compound.

Scheme SI-1. Unsuccessful results of the preparation of *N*-Boc-protected oxindoles

For this reason, we had to develop an original synthetic route. After several attempts, we established an efficient route to the *N*-Boc-protected oxindoles starting from commercially available isatin **13**. Details of the synthesis of the *N*-protected oxindoles will be described in a full paper. A procedure for **5b** is given as a representative example (Scheme SI-2). Other *N*-Boc-protected substrates were synthesized in a similar manner.

Scheme SI-2. Synthesis of the substrate **5b**, **5i**

3-Hydroxy-3-phenyloxindolin-2-one (14): A solution of PhMgBr in THF (1.0 M, 13.6 mL) was added to a stirred cold (-40 °C) suspension of isatin **13** (1.0 g, 6.8 mmol) in THF (30 mL) under an atmosphere of N₂. The mixture was allowed to warm to room temperature and was stirred until isatin was consumed. The reaction mixture was diluted with ether, cooled in an ice-bath, and then quenched with 1N HCl. The

² Rajeswaran, W. G.; Cohen, L. A. *Tetrahedron*, **1998**, *54*, 11375-11380.

aqueous layer was extracted with ether, and the combined organic layers were washed with water and brine and then dried over Na₂SO₄. After the removal of solvent, purification by flash column chromatography (hexane : acetone = 4 : 1) was carried out to give **14** in 81% yield (1.24 g) as an orange solid.

¹H-NMR (400 MHz, CD₃OD) δ 6.97 (d, *J* = 7.8 Hz, 1H), 7.04 (dt, *J* = 0.96, 7.6 Hz, 1H), 7.17 (d, *J* = 7.3 Hz, 1H), 7.26-7.33 (m, 4H), 7.35-7.38 (m, 2H).

1-(tert-Butoxycarbonyl)-2-oxo-3-phenylindolin-3-yl tert-butyl carbonate (15): **14** (29.7 mg, 0.132 mmol) was dissolved in CH₂Cl₂ (1.3 mL). To this solution were added DMAP (1.6 mg, 0.0132 mmol) and (Boc)₂O (33 mg, 0.153 mmol) at room temperature, and then the mixture was stirred for 3 h. The reaction mixture was diluted with ethyl acetate, and then quenched with saturated aqueous NH₄Cl. The aqueous layer was extracted with ethyl acetate, and the combined organic layers were washed with water and brine and then dried over Na₂SO₄. After the removal of solvent, purification by flash column chromatography (hexane : ethyl acetate = 3 : 1) was carried out to give **15** in 93% yield (44.6 mg).

¹H-NMR (400 MHz, CDCl₃) δ 1.38 (s, 9H), 1.60 (s, 9H), 7.24 (dt, *J* = 0.96, 7.6 Hz, 1H), 7.29-7.34 (m, 6H), 7.45 (ddd, *J* = 1.7, 7.6, 9.0 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H).

tert-Butyl 2-oxo-3-phenylindoline-1-carboxylate (5b): **15** (42.1 mg, 0.116 mmol) was dissolved in methanol (2 mL). Pd/C (20 mg) was added to this solution, and the resulting mixture was stirred under hydrogen atmosphere (balloon) for 3 h at room temperature. The reaction mixture was passed through celite to remove Pd/C, and the residue was washed with ether. After the removal of solvent, the crude product was purified by flash column chromatography (hexane : acetone = 12 : 1) to give **5b** in 80% yield (28.7 mg) as a white solid.

¹H-NMR (400 MHz, CDCl₃) δ 1.63 (s, 9H), 4.72 (s, 1H), 7.14-7.20 (m, 4H), 7.24-7.38 (m, 4H), 7.93 (d, *J* = 8.3 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.0, 52.5, 84.4, 115.1, 124.6, 125.1, 127.4, 127.9, 128.6, 128.9, 136.3, 140.5, 149.4, 173.9; FAB-MS (*m*NBA) *m/z* 309 (M)⁺; FAB-HRMS (*m*NBA) Calcd for C₁₉H₁₉NO₃ (M)⁺ 309.1365. Found 309.1354.

tert-Butyl 3-(2-methoxyphenyl)-2-oxoindoline-1-carboxylate (5c): ¹H-NMR (400 MHz, CDCl₃) δ 1.61 (s, 9H), 3.64 (s, 3H), 4.86 (s, 1H), 6.83 (d, *J* = 8.3 Hz, 1H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.19-7.25 (m, 2H), 7.82 (d, *J* = 8.1 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.0, 55.7, 83.9, 111.6, 114.6, 120.9, 123.9, 124.2, 125.9, 127.9, 128.3, 129.2, 130.4, 140.1, 149.5, 157.2, 174.6; FAB-MS (*m*NBA) *m/z* 339 (M)⁺; FAB-HRMS (*m*NBA) Calcd for C₂₀H₂₁NO₄ (M)⁺ 339.1471. Found 339.1474.

tert-Butyl 3-(4-methylphenyl)-2-oxoindoline-1-carboxylate (5f): ¹H-NMR (400 MHz, CDCl₃) δ 1.62 (s, 9H), 2.33 (s, 3H), 4.69 (s, 1H), 7.07-7.09 (m, 2H), 7.14-7.16 (m, 4H), 7.32-7.39 (m, 1H), 7.92 (d, *J* = 8.3 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 21.1, 28.1, 52.2, 84.3, 115.0, 124.5, 125.0, 127.6, 128.4, 128.5, 129.6, 133.2, 137.6, 140.5, 149.4, 174.1; FAB-MS (*m*NBA) *m/z* 323 (M)⁺; FAB-HRMS (*m*NBA) Calcd for C₂₀H₂₁NO₃ (M)⁺ 323.1521. Found 323.1525.

tert-Butyl 3-(4-fluorophenyl)-2-oxoindoline-1-carboxylate (5g): $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.69 (s, 9H), 4.79 (s, 1H), 7.06-7.12 (m, 2H), 7.19-7.27 (m, 4H), 7.41-7.46 (m, 1H), 8.00 (d, J = 8.3 Hz, 1H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 28.0, 51.6, 84.4, 115.1, 115.7, 115.9, 124.6, 124.9, 127.0, 128.7, 130.1, 130.2, 131.9 (d, J = 3.3 Hz), 140.4, 149.2, 162.4 (d, J = 245.2 Hz), 173.7; FAB-MS (*mNBA*) m/z 327 (M^+); FAB-HRMS (*mNBA*) Calcd for $\text{C}_{19}\text{H}_{18}\text{FNO}_3$ (M^+) 327.1271. Found 327.1264.

tert-Butyl 6-(trifluoromethyl)-3-(2-methoxyphenyl)-2-oxoindoline-1-carboxylate (5h): This compound was unexpectedly obtained during the preparation of **7**. As shown in Scheme SI-3, hydrogenolysis of **16** using Pd/C was unsuccessful. In contrast, hydrogenolysis proceeded when $\text{Pd}(\text{OH})_2$ was used. However, removal of a chlorine atom also occurred, affording **5h** in 63% yield.

Scheme SI-3. Synthesis of **5h**

5h: The di-Boc compound **16** (100 mg, 0.179 mmol), which was synthesized according to the representative procedure, was dissolved in ethyl acetate (6 mL) and methanol (6 mL). $\text{Pd}(\text{OH})_2/\text{C}$ (37.7 mg) was added to this solution, and the resulting mixture was stirred under hydrogen atmosphere (balloon) for 1 h at room temperature. The reaction mixture was passed through celite to remove $\text{Pd}(\text{OH})_2/\text{C}$, and the residue was washed with ethyl acetate. After the removal of solvent, the crude product was purified by flash column chromatography (hexane : ethyl acetate = 12 : 1) to give **5h** in 63% yield as a white solid (49.8 mg, 0.122 mmol).

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.67 (s, 9H), 3.67 (s, 3H), 4.88 (s, 1H), 6.88 (d, J = 8.1 Hz, 1H), 6.96 (dt, J = 1.0, 7.6 Hz, 1H), 7.11 (d, J = 7.8 Hz, 1H), 7.17 (d, J = 7.6 Hz, 1H), 7.31 (dt, J = 1.7, 8.1 Hz, 1H), 7.35 (d, J = 7.8 Hz, 1H), 8.19 (s, 1H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 28.0, 49.1, 55.7, 84.7, 111.6, 111.9 (q, J = 4.1 Hz), 121.0, 121.2 (q, J = 4.1 Hz), 124.0 (q, J = 270.7 Hz), 124.1, 124.9, 129.7, 130.7, 132.2, 140.5, 149.2, 157.0, 173.9; FAB-MS (*mNBA*) m/z 407 (M^+); FAB-HRMS (*mNBA*) Calcd for $\text{C}_{21}\text{H}_{20}\text{F}_3\text{NO}_4$ (M^+) 407.1344. Found 407.1340.

tert-Butyl 3-methyl-2-oxoindoline-1-carboxylate (5i): $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.53 (d, J = 7.6 Hz, 3H), 1.66 (s, 9H), 3.57 (q, J = 7.6 Hz, 1H), 7.17 (t, J = 7.3 Hz, 1H), 7.25 (d, J = 7.3 Hz, 1H), 7.30 (t, J = 8.0 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 15.9, 28.0, 41.0, 84.2, 114.9, 123.4, 124.3, 128.0, 129.3, 139.7, 149.3, 176.8; FAB-MS (*mNBA*) m/z 247 (M^+); FAB-HRMS (*mNBA*) Calcd for

C₁₄H₁₇NO₃ (M)⁺ 247.12078. Found 247.1213.

tert-Butyl 3-ethyl-2-oxoindoline-1-carboxylate (5j): ¹H-NMR (400 MHz, CDCl₃) δ 0.91 (t, *J* = 7.6 Hz, 3H), 1.65 (s, 9H), 1.99-2.12 (m, 2H), 3.54 (t, *J* = 5.6 Hz, 1H), 7.13-7.32 (m, 3H), 7.81 (d, *J* = 8.3 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 9.9, 24.3, 27.5, 47.0, 84.1, 115.2, 123.6, 124.2, 127.6, 128.0, 140.3, 149.3, 176.2; FAB-MS (*m*NBA) *m/z* 261 (M)⁺, 284 (M + Na)⁺; FAB-HRMS (*m*NBA) Calcd for C₁₅H₁₉NO₃Na (M + Na)⁺ 284.1263. Found 284.1274.

tert-Butyl 2-oxo-3-(2-oxopropyl)indoline-1-carboxylate (5k): ¹H-NMR (400 MHz, CDCl₃) δ 1.62 (s, 9H), 2.19 (s, 3H), 2.95 (dd, *J* = 7.9, 18.4 Hz, 1H), 3.25 (dd, *J* = 3.5, 18.4 Hz, 1H), 3.95 (dd, *J* = 3.6, 8.0 Hz, 1H), 7.08 (dt, *J* = 1.0, 7.6 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.24-7.29 (m, 1H), 7.79 (d, *J* = 8.3 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.0, 29.8, 41.5, 44.7, 84.2, 114.9, 123.5, 124.3, 127.5, 128.2, 140.0, 149.0, 175.9, 204.7; FAB-MS (*m*NBA) *m/z* 289 (M)⁺; FAB-HRMS (*m*NBA) Calcd for C₁₆H₁₉NO₄ (M)⁺ 289.1314. Found 289.1318.

tert-Butyl 3-benzyl-2-oxoindoline-1-carboxylate (5l): ¹H-NMR (400 MHz, CDCl₃) δ 1.64 (s, 9H), 2.95 (dd, *J* = 9.2, 13.8 Hz, 1H), 3.50 (dd, *J* = 4.4, 13.8 Hz, 1H), 3.82 (dd, *J* = 4.9, 9.2 Hz, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 7.13-7.17 (m, 2H), 7.20-7.30 (m, 4H), 7.74 (d, *J* = 7.8 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.0, 37.6, 47.5, 84.2, 114.8, 123.8, 124.3, 126.8, 127.1, 128.1, 128.3, 129.4, 137.3, 139.9, 149.1, 175.4; FAB-MS (*m*NBA) *m/z* 323 (M)⁺; FAB-HRMS (*m*NBA) Calcd for C₂₀H₂₁NO₃ (M)⁺ 323.1521. Found 323.1522.

tert-Butyl 3-isobutyl-2-oxoindoline-1-carboxylate (5m): ¹H-NMR (400 MHz, CDCl₃) δ 0.88 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H), 1.57 (s, 1H), 1.60-1.66 (m, 1H), 1.76-1.83 (m, 1H), 1.98 (sept, *J* = 6.8 Hz, 1H), 3.47 (t, *J* = 7.0 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 7.16 (d, *J* = 7.3 Hz, 1H), 7.19-7.23 (m, 1H), 7.75 (d, *J* = 8.0 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 22.3, 22.6, 25.1, 28.1, 40.8, 44.0, 84.1, 114.9, 123.8, 124.1, 127.9, 128.5, 139.8, 149.3, 176.5; FAB-MS (*m*NBA) *m/z* 289 (M)⁺; FAB-HRMS (*m*NBA) Calcd for C₁₇H₂₃NO₃ (M)⁺ 289.1678. Found 289.1685.

2-2) Procedure for the synthesis of other *N*-alkoxycarbonyl-protected oxindoles

Bulky alkoxycarbonyl groups were introduced by way of the corresponding alkoxycarbonylimidazoles such as **19** (Scheme SI-4).³ The experimental procedure for the synthesis of **5e** is given as a representative example. Full details of these reactions will be described elsewhere in due course.

³ Davies, G.; Russell, A. T.; Sanderson, A. J.; Simpson, S. J. *Tetrahedron Lett.* **1999**, *40*, 4391-4394.

Scheme SI-4. Synthesis of **5d,e**

17: This compound was prepared according to the synthetic method for **14**. After the similar aqueous workup, recrystallization of the crude product from hexane-CH₂Cl₂ afforded **17** as a white solid (84%).

¹H-NMR (400 MHz, DMSO) δ 3.39 (s, 3H), 6.41 (s, 1H), 6.75-6.82 (m, 3 H), 6.87 (d, *J* = 7.8 Hz, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 7.15 (dt, *J* = 1.5, 7.3 Hz, 1H), 7.27 (dt, *J* = 1.7, 7.8 Hz, 1H), 7.83 (dd, *J* = 1.72, 7.6 Hz, 1H), 10.3 (s, 1H); ¹³C-NMR (400 MHz, DMSO) δ 55.5, 74.9, 109.0, 111.7, 120.3, 121.1, 123.6, 126.9, 128.6, 128.7, 130.4, 133.0, 143.0, 155.6, 178.4.

18: 10% Pd/C (106 mg) was added to a solution of **17** (255 mg, 1 mmol) in MeOH (15 mL). The reaction mixture was stirred under hydrogen atmosphere (balloon) for 8 h at room temperature. After filtration, evaporation under reduced pressure, followed by recrystallization from hexane-CHCl₃ gave pure **18** as a white solid (85%, 203 mg).

¹H-NMR (400 MHz, CDCl₃) δ 3.75 (s, 3H), 4.92 (s, 1H), 6.89-6.95 (m, 4H), 7.01 (d, *J* = 7.3 Hz, 1H), 7.11-7.19 (m, 2H), 7.26-7.30 (m, 1H), 9.03 (s, 1H); ¹³C-NMR (400 MHz, DMSO) δ 48.5, 55.7, 109.5, 111.5, 121.0, 122.3, 124.3, 125.6, 127.8, 129.0, 130.2, 130.5, 141.5, 157.5, 179.6.

19: To a stirred solution of 9-fluorenone (1.1 g, 6 mmol) in CH₃CN (40 mL) was added carbonyl diimidazole (2 g, 12.3 mmol) at room temperature. After 24 h, solvent was removed under reduced pressure. The resulting crude product was further purified by flash column chromatography (hexane : ethyl acetate = 2 : 1) to give **19** as a white solid (1.6 g, 97%).

¹H-NMR (400 MHz, CDCl₃) δ 6.90 (s, 1H), 7.07 (s, 1H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.45-7.49 (m, 4H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.71 (d, *J* = 7.3 Hz, 2H), 8.15 (s, 1H).

5e: To a stirred solution of **18** (75 mg, 0.313 mmol) in dry THF (1.6 mL) was added EtMgBr (0.98 M in THF, 0.32 mL, 0.313 mmol) at $-40\text{ }^{\circ}\text{C}$. After 10 min, a solution of **19** (95 mg, 0.34 mmol) in THF (1.6 mL) was added to the reaction vessel at $-40\text{ }^{\circ}\text{C}$ and the resulting mixture was allowed to stir at room temperature for additional 2 h. Under ice-bath cooling, saturated aqueous NH_4Cl was added for quenching. The aqueous layer was extracted by ethyl acetate several times, and the combined organic layers were washed with brine. After removal of solvent under reduced pressure, purification by flash column chromatography (hexane : ethyl acetate = 5 : 1) afforded **5e** in 70% yield as a white solid.

¹H-NMR (400 MHz, CDCl_3) δ 3.64 (s, 3H), 4.91 (s, 1H), 6.85 (d, J = 8.0 Hz, 1H), 6.93 (dt, J = 1.0, 7.6 Hz, 1H), 6.96 (s, 1H), 7.01 (d, J = 7.3 Hz, 1H), 7.07 (dt, J = 1.0, 7.6 Hz, 1H), 7.15 (d, J = 6.8 Hz, 1H), 7.22-7.34 (m, 4H), 7.43 (t, J = 7.3 Hz, 2H), 7.69 (t, J = 7.3 Hz, 2H), 7.75-7.78 (m, 2H), 7.80 (d, J = 8.0 Hz, 1H); ¹³C-NMR (100 MHz, CDCl_3) δ 49.0, 55.7, 77.8, 111.7, 114.8, 120.1, 121.0, 124.1, 124.6, 125.6, 126.2, 126.3, 128.0, 128.1, 128.4, 129.4, 129.8, 130.6, 1309.5, 141.1, 141.2, 151.8, 157.1, 174.3; FAB-MS (*m*NBA) m/z 447 (M)⁺, 470 ($\text{M} + \text{Na}$)⁺; FAB-HRMS (*m*NBA) Calcd for $\text{C}_{29}\text{H}_{21}\text{NO}_4\text{Na}$ ($\text{M} + \text{Na}$)⁺ 470.4813. Found 470.1347.

5d: ¹H-NMR (400 MHz, CDCl_3) δ 3.58 (s, 3H), 4.90 (s, 1H), 6.87 (d, J = 8.3 Hz, 1H), 6.95-7.09 (m, 4H), 7.19-7.39 (m, 9H), 7.56-7.58 (m, 4H), 7.96 (d, J = 8.3 Hz, 1H); ¹³C-NMR (400 MHz, CDCl_3) δ 49.4, 55.6, 80.1, 111.7, 114.9, 121.0, 123.8, 124.6, 125.7, 126.5, 126.9, 127.0, 127.6, 127.9, 128.0, 128.1, 128.4, 128.5, 128.6, 128.6, 129.5, 130.9, 139.8, 139.9, 150.5, 157.1, 174.5; FAB-MS (*m*NBA) m/z 449 (M)⁺, 472 ($\text{M} + \text{Na}$)⁺; FAB-HRMS (*m*NBA) Calcd for $\text{C}_{29}\text{H}_{23}\text{NO}_4\text{Na}$ ($\text{M} + \text{Na}$)⁺ 472.1525. Found 472.1512.

3) General procedure for the catalytic enantioselective fluorination of oxindoles

The oxindole **5** (0.2 mmol) was dissolved in the indicated solvent (IPA or acetone) (0.2 mL ~ 0.4 mL). To this solution was added the palladium complex **1** (0.01 mmol) or **2** (0.005 mmol), and successively NFSI (94 mg, 0.3 mmol) was added at the given temperature (0 $^{\circ}\text{C}$ or rt). The reaction mixture was stirred at the same temperature. After the completion of the reaction (TLC, benzene/ether = 5/1, hexane/ether = 5/1, hexane/ethyl acetate = 6/1, etc.), saturated aqueous NH_4Cl (3 mL) was added for quenching. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with water and brine. After drying over Na_2SO_4 , solvent was removed under reduced pressure. Further purification was performed by flash column chromatography on SiO_2 (hexane-ethyl acetate system) to give the pure product **6**. The ee of the product was determined by chiral HPLC analysis.

4) Details of the optimization of the reaction conditions

In addition to Table 1, full data of the optimization of the reaction conditions were summarized in Table SI-1. Among the solvents tested, 2-propanol (IPA) and acetone gave high enantioselectivity in the case of **5b** (entries 2-7). In contrast, in the case of **5c** and **7**, acetone gave better enantioselectivity than IPA (entries 9-10) (see also Table SI-2). Thus, acetone was chosen for further experiments aiming at the asymmetric synthesis of BMS compound **3** (see Table 2, Scheme 1). For **5i**, IPA was best in view of chemical yield while enantioselectivity was not affected by the solvents significantly (entries 13-15).

As for the ligand structure, the bulkier DM-BINAP was more effective than BINAP. Although distinct difference of the ee values was not observed in the case of **5b** (entries 1,2), the ees of **6c** and **6i** were significantly improved when (*S*)-DM-BINAP was used (entries 8 vs 9, and 11 vs 12).

In general, the palladium complex **2** was superior to **1** in terms of both the chemical yield and enantioselectivity. A particular case was the reaction of **5i**. While the reaction of **5i** in the presence of the Pd complex **1** consisting of (*S*)-DM-BINAP proceeded in 58% yield with 80% ee (entry 12), the Pd complex **2** gave the desired product **6j** in better yield of 75% with better enantioselectivity of 95% (entry 13).

Table SI-1. Details of the optimization of the reaction conditions

5 (racemate) + NFSI (1.5 eq) $\xrightarrow[\text{solvent, rt}]{\text{Pd-cat. (5 mol\% Pd)}}$ 6

entry	Pd-cat.	Ligand	5(R)	solvent	time (h)	yield (%)	ee ^a (%)
1	1	(<i>R</i>)-BINAP	5b (Ph)	THF	12	48	77
2	1	(<i>S</i>)-DM-BINAP	5b	THF	12	53	81
3	1	(<i>S</i>)-DM-BINAP	5b	CH ₂ Cl ₂		decomposition	
4	1	(<i>S</i>)-DM-BINAP	5b	DMF	12	53	18
5	1	(<i>S</i>)-DM-BINAP	5b	IPA	3	66	88
6	1	(<i>S</i>)-DM-BINAP	5b	acetone	3	58	89
7	2	(<i>S</i>)-DM-BINAP	5b	IPA	5	90	88
8	1	(<i>R</i>)-BINAP	5c (<i>o</i> -MeOC ₆ H ₄)	IPA	12	95	20
9	1	(<i>S</i>)-DM-BINAP	5c	IPA	12	70	69
10	2	(<i>S</i>)-DM-BINAP	5c	acetone	18	89	76
11	1	(<i>R</i>)-BINAP	5i (Me)	THF	8	45	29
12	1	(<i>S</i>)-DM-BINAP	5i	THF	7	58	80
13	2	(<i>S</i>)-DM-BINAP	5i	THF	3	75	95
14	2	(<i>S</i>)-DM-BINAP	5i	EtOH	5	54	96
15	2	(<i>S</i>)-DM-BINAP	5i	IPA	5	86	95

^a Determined by chiral HPLC analysis.

5) Characterization of the fluorinated products **6**

tert-Butyl 3-fluoro-2-oxo-3-phenylindoline-1-carboxylate (6b): ¹H-NMR (400 MHz, CDCl₃) δ 1.62 (s, 9H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.34-7.41 (m, 6H), 7.51 (tt, *J* = 1.7, 8.0 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.0, 85.0, 92.7 (d, *J* = 183.5 Hz), 115.6, 125.3 (d, *J* = 2.5 Hz), 125.4 (d, *J* = 18.9 Hz), 126.2, 126.3, 128.6, 129.5, 131.8 (d, *J* = 2.4 Hz), 135.6 (d, *J* = 27.2 Hz), 140.9 (d, *J* = 4.9 Hz), 148.9, 170.1 (d, *J* = 28.0 Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -69.3; FAB-MS (*m*NBA) *m/z* 328 (M+1)⁺, 272 (M+2H-tBu)⁺; [α]_D²⁷ -70.4 (c = 0.77, CHCl₃) (79% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 299 / 1, 0.25 mL / min, 254 nm) *t*_r(major) = 44.8 min, *t*_r (minor) = 55.6 min; FAB-HRMS (*m*NBA) Calcd for C₁₉H₁₉O₃NF (M+1)⁺ 328.1349. Found 328.1352, IR (solid) 2981, 2931, 1779, 1733, 1609, 1469, 1369, 1342, 1286, 1247, 1145, 1098, 1001, 837, 754, 720, 694, 627 cm⁻¹.

tert-Butyl 3-fluoro-3-(2-methoxyphenyl)-2-oxoindoline-1-carboxylate (6c): ¹H-NMR (400 MHz, CDCl₃) δ 1.66 (s, 9H), 3.53 (s, 3H), 6.81 (d, *J* = 8.0 Hz, 1H), 7.08-7.14 (m, 3H), 7.32-7.42 (m, 2H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.1, 55.8, 84.4, 91.7 (d, *J* = 181.8 Hz), 111.6 (d, *J* = 1.6 Hz), 115.1, 121.1, 124.6 (d, *J* = 3.2 Hz), 124.9, 125.8 (d, *J* = 10.7 Hz), 125.8 (d, *J* = 11.6 Hz), 126.0, 130.2, 131.2 (d, *J* = 3.3 Hz), 141.0 (d, *J* = 4.9 Hz), 149.2, 154.8 (d, *J* = 6.5 Hz), 170.5 (d, *J* = 20.6 Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -75.9; FAB-MS (*m*NBA) *m/z* 358 (M+1)⁺, 302 (M+2H-tBu)⁺; [α]_D²⁷ +106.5 (c = 0.92, CHCl₃) (70% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 99 / 1, 0.4 mL / min, 254 nm) *t*_r (major) = 23.8 min, *t*_r (minor) = 39.8 min; FAB-HRMS (*m*NBA) Calcd for C₂₀H₂₀O₄NF (M)⁺ 357.1376. Found 357.1375, Calcd for C₁₅H₁₉O₃NF (M+1)⁺ 358.1455. Found 358.1455; IR (solid) 2923, 2843, 1785, 1730, 1606, 1465, 1369, 1344, 1290, 1247, 1147, 1097, 1001, 840, 753, 626 cm⁻¹.

tert-butyl 3-fluoro-3-(4-methylphenyl)-2-oxoindoline-1-carboxylate (6f): ¹H-NMR (400 MHz, CDCl₃) δ 1.61 (s, 9H), 2.35 (s, 3H), 7.18-7.20 (m, 2H), 7.24-7.29 (m, 3H), 7.36-7.38 (m, 1H), 7.48-7.52 (m, 1H), 8.00 (d, *J* = 8.3 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 21.2, 28.0, 84.9, 92.6 (d, *J* = 186.8 Hz), 115.6, 125.2 (d, *J* = 2.5 Hz), 125.6 (d, *J* = 17.3 Hz), 126.2 (d, *J* = 2.5 Hz), 126.3, 129.3, 131.7 (d, *J* = 3.0 Hz), 132.6 (d, *J* = 28.0 Hz), 139.6, 140.9 (d, *J* = 5.0 Hz), 148.9, 170.3 (d, *J* = 25.5 Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -68.5; FAB-MS (*m*NBA) *m/z* 341 (M)⁺, 286 (M+2H-tBu)⁺; [α]_D²⁶ -70.7 (c = 0.685, CHCl₃) (85% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 99 / 1, 1.0 mL / min, 254 nm) *t*_r (major) = 5.3 min, *t*_r (minor) = 6.3 min; FAB-HRMS (*m*NBA) Calcd for C₂₀H₂₀NO₃F (M)⁺ 341.1427. Found 341.1430; IR (neat) 2981, 1782, 1733, 1610, 1466, 1343, 1286, 1248, 1145, 1097, 1002, 816, 752 cm⁻¹.

tert-butyl 3-fluoro-3-(4-fluorophenyl)-2-oxoindoline-1-carboxylate (6g): ¹H-NMR (400 MHz, CDCl₃) δ 1.62 (s, 9H), 7.07 (t, *J* = 8.7 Hz, 2H), 7.26-7.31 (m, 1H), 7.34-7.38 (m, 3H), 7.52 (tt, *J* = 1.7, 8.0 Hz, 2H), 8.01 (d, *J* = 8.7 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.0, 85.2, 92.2 (d, *J* = 186.8 Hz), 115.5, 115.8, 125.1 (d, *J* = 17.3 Hz), 125.4 (d, *J* = 2.5 Hz), 126.2, 128.5 (d, *J* = 5.8 Hz), 128.6 (d, *J* = 5.8 Hz), 131.2 (d, *J* = 3.3 Hz), 131.5 (d, *J* = 3.3 Hz), 132.0 (d, *J* = 3.3 Hz), 141.0 (d, *J* = 5.7 Hz), 148.9, 163.5 (dd, *J* = 2.5, 248.2 Hz), 170.0 (d, *J* = 25.5 Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -66.9, -35.5 – -35.4 (m); FAB-MS (*m*NBA) *m/z*

345 (M)⁺; $[\alpha]_D^{26}$ -93.0 (c = 1.04, CHCl₃) (84% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 99 / 1, 1.0 mL / min, 254 nm) t_r (major) = 5.3 min, t_r (minor) = 6.6 min; FAB-HRMS (*mNBA*) Calcd for C₁₉H₁₇O₃NF₂ (M)⁺ 345.1177. Found 345.1168, Calcd for C₁₉H₁₈O₃NF₂ (M+1)⁺ 346.1255. Found 346.125; IR (neat) 2982, 1782, 1735, 1608, 1466, 1343, 1286, 1248, 1145, 1095, 1001, 833, 756 cm⁻¹.

***tert*-Butyl 3-fluoro-6-(trifluoromethyl)-3-(2-methoxyphenyl)-2-oxoindoline-1-carboxylate (6h):** ¹H-NMR (400 MHz, CDCl₃) δ 1.67 (s, 9H), 3.55 (s, 3H), 6.82 (d, *J* = 8.3 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.35-7.40 (m, 2H), 7.80 (d, *J* = 7.8 Hz, 1H), 8.25 (s, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.0, 55.7, 85.2, 91.0 (d, *J* = 184.3 Hz), 111.5 (d, *J* = 2.5 Hz), 112.5 (d, *J* = 2.5 Hz), 121.3, 121.7 (m), 123.6 (q, *J* = 270.7 Hz), 124.9 (d, *J* = 28.0 Hz), 125.2, 125.8 (d, *J* = 12.3 Hz), 129.4 (d, *J* = 18.1 Hz), 130.6, 133.2 (dq, *J* = 2.5, 32.1 Hz), 141.4 (d, *J* = 4.9 Hz), 148.9, 154.7 (d, *J* = 6.6 Hz), 169.7 (d, *J* = 20.6 Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -78.1, 13.3; FAB-MS (*mNBA*) *m/z* 426 (M+1)⁺, 370 (M+2H-tBu)⁺; $[\alpha]_D^{28}$ +93.9 (c = 0.45, CHCl₃) (75% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 299 / 1, 1.0 mL / min, 254 nm) t_r (major) = 14.2 min, t_r (minor) = 33.3 min; FAB-HRMS (*mNBA*) Calcd for C₁₄H₁₆O₃NF (M+1)⁺ 426.1328. Found 426.1337; IR (solid) 2925, 2843, 1794, 1736, 1600, 1493, 1439, 1359, 1320, 1297, 1240, 1149, 1062, 960, 891, 842, 755 cm⁻¹.

***tert*-Butyl 3-fluoro-3-methyl-2-oxoindoline-1-carboxylate (6i):** ¹H-NMR (400 MHz, CDCl₃) δ 1.65 (s, 9H), 1.79 (d, *J* = 22.0 Hz, 3H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.41-7.48 (m, 2H), 7.90 (d, *J* = 8.1 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 21.8 (d, *J* = 30.4 Hz), 28.0, 85.0, 90.3 (d, *J* = 183.4 Hz), 115.6, 124.1, 125.1 (d, *J* = 2.5 Hz), 126.2 (d, *J* = 18.9 Hz), 131.4 (d, *J* = 2.5 Hz), 139.7 (d, *J* = 4.9 Hz), 148.8, 171.2 (d, *J* = 22.2 Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -69.0 (q, *J* = 22.0 Hz); FAB-MS (*mNBA*) *m/z* 266 (M+1)⁺, 210 (M+2H-tBu)⁺; $[\alpha]_D^{26}$ +3.7 (c = 1.72, CHCl₃) (90% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 99 / 1, 0.5 mL / min, 254 nm) t_r (minor) = 12.1 min, t_r (major) = 13.8 min; FAB-HRMS (*mNBA*) Calcd for C₁₄H₁₆O₃NF (M)⁺ 265.1114. Found 265.1114; IR (neat) 2983, 2927, 1783, 1731, 1611, 1481, 1469, 1370, 1346, 1283, 1248, 1140, 1104, 1005, 907, 838, 762, 683, 568, 554 cm⁻¹.

***tert*-Butyl 3-ethyl-3-fluoro-2-oxoindoline-1-carboxylate (6j):** ¹H-NMR (400 MHz, CDCl₃) δ 0.85 (t, *J* = 7.6 Hz, 3H), 1.65 (s, 9H), 2.14-2.27 (m, 2H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.41-7.45 (m, 2H), 7.90 (d, *J* = 8.6 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 7.0 (d, *J* = 7.4 Hz), 28.0, 28.8 (d, *J* = 28.0 Hz), 84.9, 93.3 (d, *J* = 186.7 Hz), 115.5, 124.4, 124.8 (d, *J* = 21.4 Hz), 125.0 (d, *J* = 2.4 Hz), 131.3 (d, *J* = 2.5 Hz), 140.3 (d, *J* = 5.8 Hz), 148.8, 171.2 (d, *J* = 21.4 Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -73.9 (t, *J* = 13.9 Hz); FAB-MS (*mNBA*) *m/z* 280 (M+1)⁺, 224 (M+2H-tBu)⁺; $[\alpha]_D^{28}$ +25.4 (c = 0.90, CHCl₃) (92% ee); HPLC (DAICEL CHIRALCEL OJ-H, hexane / IPA = 99/1, 0.5 mL / min, 254 nm) t_r (minor) = 13.1 min, t_r (major) = 17.5 min; FAB-HRMS (*mNBA*) Calcd for C₁₅H₁₈O₃NF (M)⁺ 279.1271. Found 279.1277, Calcd for C₁₅H₁₉O₃NF (M+1)⁺ 280.1349. Found 280.1353; IR (neat) 2980, 2935, 1782, 1736, 1608, 1480, 1467, 1350, 1285, 1246, 1143, 1084, 1001, 934, 839, 759, 681 cm⁻¹.

***tert*-Butyl 3-fluoro-3-(2-oxopropyl)-2-oxoindoline-1-carboxylate (6k):** ¹H-NMR (400 MHz, CDCl₃) δ 1.65 (s, 9H), 2.12 (s, 3H), 3.52-3.65 (m, 2H), 7.17-7.21 (m, 1H), 7.35-7.38 (m, 1H), 7.41-7.46 (m, 1H), 7.94 (d, *J* = 8.3 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.5, 30.1 (d, *J* = 3.2 Hz), 48.7 (d, *J* = 28.8 Hz), 84.7, 89.6 (d, *J* = 179.4 Hz), 115.6 (d, *J* = 2.5 Hz), 123.8 (d, *J* = 1.7 Hz), 124.1 (d, *J* = 17.3 Hz), 124.7 (d, *J* = 3.3 Hz), 131.8 (d, *J* = 3.3 Hz), 141.5 (d, *J* = 6.6 Hz), 148.8, 170.1 (d, *J* = 19.8 Hz), 203.0 (d, *J* = 12.3 Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -71.1 (t, *J* = 8.1 Hz); FAB-MS (*mNBA*) *m/z* 307 (M)⁺, 252 (M+2H-tBu)⁺;

$[\alpha]_D^{25} +37.8$. (c = 0.62, CHCl₃) (85% ee); HPLC (DAICEL CHIRALCEL AD-H, hexane / IPA = 99 / 1, 1.0 mL / min, 254 nm) t_r (minor) = 21.9 min, t_r (major) = 27.4 min; FAB-HRMS (*mNBA*) Calcd for C₁₆H₁₉O₄NF (M+1)⁺ 308.1298. Found 308.1297; IR (neat) 3120, 2981, 1780, 1717, 1612, 1469, 1349, 1288, 1251, 1097, 840, 748 cm⁻¹.

***tert*-Butyl 3-benzyl-3-fluoro-2-oxoindoline-1-carboxylate (6l):** ¹H-NMR (400 MHz, CDCl₃) δ 1.60 (s, 9H), 3.24 (dd, *J* = 13.4, 22.2 Hz, 1H), 3.57 (dd, *J* = 10.0, 13.4 Hz, 1H), 6.99 (m, 3H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.16-7.22 (m, 3H), 7.35 (tt, *J* = 1.5, 8.0 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.0, 42.0 (d, *J* = 28.0 Hz), 84.8, 92.6 (d, *J* = 190.8 Hz), 115.2, 124.1 (d, *J* = 18.9 Hz), 124.5 (d, *J* = 2.5 Hz), 125.2, 127.4, 128.2, 130.6, 131.2 (d, *J* = 3.3 Hz), 132.0 (d, *J* = 6.6 Hz), 140.0 (d, *J* = 4.9 Hz), 148.5, 171.2 (d, *J* = 20.6 Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -74.2 (dd, *J* = 10.0, 22.2 Hz); FAB-MS (*mNBA*) *m/z* 342 (M+1)⁺, 286 (M+2H-*t*Bu)⁺; $[\alpha]_D^{27} -33.5$ (c = 0.75, CHCl₃) (80% ee); HPLC (DAICEL CHIRALCEL OJ-H, hexane / IPA = 99 / 1, 0.7 mL / min, 254 nm) t_r (minor) = 12.6 min, t_r (major) = 17.1 min; FAB-HRMS (*mNBA*) Calcd for C₁₄H₁₆O₃NF (M+1)⁺ 342.1505. Found 342.1508; IR (neat) 2981, 2927, 1778, 1736, 1610, 1480, 1467, 1369, 1348, 1286, 1249, 1146, 1004, 931, 838, 745, 699, 607, 574, 537 cm⁻¹.

***tert*-Butyl 3-fluoro-3-isobutyl-2-oxoindoline-1-carboxylate (6m):** ¹H-NMR (400 MHz, CDCl₃) δ 0.82 (d, *J* = 6.6 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 1.58-1.66 (m, 1H), 1.64 (s, 9H), 2.05-2.20 (m, 2H), 7.21-7.25 (m, 1H), 7.41-7.46 (m, 2H), 7.88-7.91 (m, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 23.3, 23.6, 23.7, 28.0, 43.6 (d, *J* = 25.5 Hz), 84.9, 92.9 (d, *J* = 186.8 Hz), 115.5, 124.8, 124.8 (d, *J* = 3.3 Hz), 125.2 (d, *J* = 18.9 Hz), 131.3 (d, *J* = 3.3 Hz), 140.2 (d, *J* = 5.8 Hz), 148.8, 171.3 (d, *J* = 23.0 Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -67.5 (t, *J* = 14.9 Hz); FAB-MS (*mNBA*) *m/z* 307 (M)⁺, 252 (M+2H-*t*Bu)⁺; $[\alpha]_D^{25} +26.1$ (c = 0.63, CHCl₃) (68% ee); HPLC (DAICEL CHIRALCEL AD-H, hexane / IPA = 200 / 1, 1.0 mL / min, 254 nm) t_r (major) = 5.3 min, t_r (minor) = 5.8 min; IR (neat) 2961, 1782, 1733, 1612, 1467, 1349, 1287, 1250, 1143, 841, 770 cm⁻¹; Anal. Calcd for C₁₇H₂₂FNO₃: C, 66.43. H, 7.21. N, 4.56. Found: C, 66.53. H, 7.32. N, 4.46.

6d: ¹H-NMR (400 MHz, CDCl₃) δ 3.36 (s, 3H), 6.79 (d, *J* = 8.3 Hz, 1H), 7.07-7.16 (m, 4H), 7.25-7.42 (m, 9H), 7.55-7.60 (m, 4H), 7.83 (d, *J* = 7.6 Hz, 3H), 8.01 (d, *J* = 8.3 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 55.6, 80.3, 91.6 (d, *J* = 183.0 Hz), 111.5 (d, *J* = 1.6 Hz), 115.3 (d, *J* = 1.7 Hz), 121.2, 124.9, 125.0 (d, *J* = 3.3 Hz), 125.5, 125.7, 125.8, 125.9, 126.0, 126.9 (d, *J* = 15.6 Hz), 128.0, 128.6 (d, *J* = 4.1 Hz), 130.3, 131.3 (d, *J* = 4.1 Hz), 139.5, 140.5 (d, *J* = 5.7 Hz), 150.1, 154.7, 154.8, 170.3 (d, *J* = 20.6 Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -75.6; FAB-MS (*mNBA*) *m/z* 467 (M)⁺, 468 (M+1)⁺; HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 90 / 10, 1.0 mL / min, 254 nm) t_r (major) = 6.0 min, t_r (minor) = 14.0 min; FAB-HRMS (*mNBA*) Calcd for C₂₉H₂₃O₄NF (M+1)⁺ 468.1611. Found 468.1599.

6e: ¹H-NMR (400 MHz, CDCl₃) δ 3.47 (s, 3H), 6.77 (d, *J* = 8.7 Hz, 1H), 6.96 (s, 1H), 7.09-7.13 (m, 3H), 7.31-7.39 (m, 4H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.70 (d, *J* = 7.6 Hz, 2H), 7.75-7.80 (m, 3H), 7.87 (d, *J* = 8.3 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 55.8, 78.1, 91.5 (d, *J* = 182.7 Hz), 111.5 (d, *J* = 1.7 Hz), 115.3 (d, *J* = 1.7 Hz), 120.2 (d, *J* = 1.7 Hz), 121.1, 125.0, 125.1, 125.5, 125.8 (d, *J* = 11.5 Hz), 125.9 (d, *J* = 20.7 Hz),

126.1, 126.2, 127.9, 128.0, 129.9, 130.3, 131.3 (d, $J = 4.1$ Hz), 140.3 (d, $J = 5.8$ Hz), 140.9, 141.0, 141.1, 141.2, 151.5, 154.7, 154.8, 170.2 (d, $J = 19.6$ Hz); ^{19}F -NMR (376 MHz, CDCl_3) δ -75.5; FAB-MS (*mNBA*) m/z 365 (M) $^+$, 366 ($\text{M}+1$) $^+$; HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 95 / 5, 1.0 mL / min, 254 nm) t_r (minor) = 35.3 min, t_r (major) = 45.6 min; FAB-HRMS (*mNBA*) Calcd for $\text{C}_{29}\text{H}_{21}\text{O}_4\text{NF}$ ($\text{M}+1$) $^+$ 466.1455. Found 466.1461.

6) Conversion of **6i**

Scheme SI-5.

To a stirred solution of **6i** (15 mg, 0.057 mmol, 96% ee) in dry MeOH (1 mL) was added MeONa (1 mg, 0.0185 mmol) at 0 °C. After 1 h, saturated aqueous NH_4Cl was added for quenching. After usual workup, purification by flash column chromatography (hexane : ethyl acetate = 8 : 1) afforded the desired product **9** in 95% yield (16.0 mg, colorless oil) without loss of enantioselectivity.

9: ^1H -NMR (400 MHz, CDCl_3) δ 1.52 (s, 9H), 2.02 (d, $J = 23.2$ Hz, 3H), 3.75 (s, 3H), 7.12 (tt, $J = 1.2, 7.62$ Hz, 1H), 7.25-7.35 (m, 1H), 7.37-7.42 (m, 2H), 7.88 (d, $J = 8.3$ Hz, 1H); ^{13}C -NMR (100 MHz, CDCl_3) δ 23.0 (d, $J = 24.7$ Hz), 28.3, 53.1, 80.4, 94.8 (d, $J = 178.5$ Hz), 123.6, 126.0, 126.1, 127.7 (d, $J = 15.0$ Hz), 130.2, 136.9, 153.1, 171.6 (d, $J = 26.4$ Hz); ^{19}F -NMR (376 MHz, CDCl_3) δ -65.5 (q, $J = 23.2$ Hz); FAB-MS (*mNBA*) m/z 297 (M) $^+$, 298 ($\text{M}+1$) $^+$, 242 ($\text{M}+2\text{H}-t\text{Bu}$) $^+$; $[\alpha]_D^{26}$ -50.8 ($c = 0.49$, CHCl_3) (96% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 95 / 5, 1.0 mL/min, 254 nm) t_r (major) = 7.2 min, t_r (minor) = 10.1 min; FAB-HRMS (*mNBA*) Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4\text{NF}$ (M) $^+$ 297.1376. Found 297.1381. Calcd for $\text{C}_{15}\text{H}_{21}\text{O}_4\text{NF}$ (M) $^+$ 298.1455. Found 298.1450; IR (neat) 3441, 2977, 1730, 1588, 1515, 1450, 1368, 1299, 1234, 1153, 1115, 1046, 1023 cm^{-1} .

7) Explanation of the stereoselectivity of this fluorination reaction

The assumed chiral Pd enolate is described in Figure SI-1. The *re*-face of the putative Pd enolate would be blocked by one of the aryl groups of the ligand, together with *t*-Bu group that might be located at the *re*-face of the enolate to avoid steric repulsion with the aryl group of the ligand. As a result, NFSI reacted preferentially from the less hindered *si*-face of the enolate. A space-filling model of this Pd enolate was generated by MM3 calculation using Cache 5.0.

Figure SI-1. Assumed chiral Pd enolate

8) Catalytic asymmetric synthesis of BMS-204352

BMS-204352 was developed as a neuroprotective agent, especially being applicable to ischemic stroke. This compound is a potent and selective opener of large-conductance calcium-activated (Maxi-K) potassium channels, which shows a brain/plasma ratio of >9 in rats. At present, optically active BMS-204352 is provided by chiral HPLC separation or chiral resolution. So far, two attempts to synthesize the enantioenriched **3** using a stoichiometric amount of chiral fluorinating reagents were reported by Shibata et al. and Cahard et al. In contrast, the catalytic synthesis of optically active **3** has not been reported. We believe that the application of our catalytic reaction to the synthesis of **3** is quite unique and promising for the future development.

8-1) Preparation of **28**

The synthesis of the compound **28** was summarized in Scheme SI-6. This compound was identical to the reported compound by comparison with ^1H NMR data.⁴

Scheme SI-6. Synthesis of **28**

⁴ (a) Hewawasam, P.; Erway, M.; Moon, S. L.; Knipe, J.; Weiner, H.; Boissard, C. G.; Post-Munson, D. J.; Gao, Q.; Huang, S.; Gribkoff, V. K.; Meanwell, N. A. *J. Med. Chem.* **2002**, *45*, 1487-1499. (b) Hewawasam, P.; Meanwell, N. A. *Tetrahedron Lett.* **1994**, *35*, 7303-7306. (c) Hewawasam, P.; Meanwell, N. A.; Gribkoff, V. K. US Patent. 5565483, **1996**. (d) Lehmler, H.-J.; Robertson, L. W. *Chemosphere*. **2001**, *45*, 1119-1127

2-Bromo-4-chloroanisole (21): **20** (5.0 g, 24.1 mmol) was dissolved in aqueous sodium hydroxide solution (2.8 M, 10.7 ml). Me_2SO_4 (2.5 ml, 26.5 mmol) was added slowly to this solution, and the formation of a white precipitate was observed. After the reaction was complete, the reaction mixture was extracted with ether. The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure to yield **21** (4.9 g, 92%) as a white solid.

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 3.86 (s, 3H), 6.80 (d, $J = 8.8$ Hz, 1H), 7.23 (dd, $J = 2.7, 8.8$ Hz, 1H), 7.52 (d, $J = 2.7$ Hz, 1H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 56.4, 112.1, 112.5, 125.9, 128.2, 132.8, 154.7.

tert-Butyl 3-(trifluoromethyl)phenylcarbamate (24): A stirred neat mixture of 3-aminobenzotrifluoride (10 mL, 80.3 mmol) and $(\text{Boc})_2\text{O}$ (18.4 g, 84.3 mmol) was heated at 80 °C for 4 h until CO_2 evolution stopped. The mixture was allowed to cool and the *t*BuOH was evaporated under reduced pressure. The resultant white solid was recrystallized from hexane to give white needles of **24** (16.3 g, 78%).

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.52 (s, 9H), 6.61 (brs, 1H), 7.27 (d, $J = 8.0$ Hz, 1H), 7.39 (t, $J = 7.8$ Hz, 1H), 7.48 (d, $J = 7.4$ Hz, 1H), 7.71 (s, 1H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 28.2, 81.2, 115.1, 119.5 (q, $J = 3.3$ Hz), 121.4, 123.9 (q, $J = 270.6$ Hz), 129.4, 131.4 (d, $J = 32.1$ Hz), 138.9, 152.4.

tert-Butyl 2-(ethyl formyl formyl)-5-(trifluoromethyl)phenylcarbamate (25): *s*-BuLi (cyclohexane-hexane solution, 0.93 M, 99 mL, purchased from KANTO CHEMICAL Co., INC.) was added to a solution of **24** (10 g, 38 mmol) in dry THF (40 mL) at -78 °C under nitrogen. The reaction mixture was warmed to -40 °C and stirred for 3 hours. The resulting thick yellow slurry of the dianion was cooled to -78 °C, and neat dry diethyl oxalate (7.4 mL, 50.1 mmol) was added rapidly. The orange-brown solution was stirred at -78 °C for additional 1 h. The reaction mixture was diluted with ether and quenched with 3N HCl. The organic layer was separated and washed with water, brine and then dried over Na_2SO_4 . Evaporation of solvents, followed by flash chromatography (hexane : acetone = 60 : 1) afforded the pure keto-ester **25** (11.9 g, 87%).

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.43 (t, $J = 7.1$ Hz, 3H), 1.55 (s, 9H), 4.48 (q, $J = 7.1$ Hz, 2H), 7.29 (d, $J = 8.3$ Hz, 1H), 7.82 (d, $J = 8.3$ Hz, 1H), 8.89 (s, 1H), 10.43 (brs, 1H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 14.0,

28.1, 62.8, 81.9, 116.3 (q, $J = 4.1$ Hz), 117.4 (q, $J = 3.3$ Hz), 118.4, 123.0 (q, $J = 272.3$ Hz), 133.9, 137.4 (q, $J = 32.1$ Hz), 143.9, 152.3, 163.0, 189.4.

6-(Trifluoromethyl)-isatin (26): A stirred solution of the keto-ester **25** (10 g, 27.7 mmol) in THF (175 mL) and 3N HCl (46 mL) was heated to reflux for 6 h. After cooling, ether was added and the organic layer was separated and washed with water and brine. Removal of the solvent by evaporation, followed by recrystallization (hexane-CH₂Cl₂) afforded **26** as an orange solid (6.5 g, 96%).

¹H-NMR (400 MHz, DMSO) δ 7.09 (s, 1H), 7.39 (d, $J = 7.8$ Hz, 1H), 7.68 (d, $J = 7.8$ Hz, 1H), 11.26 (brs, 1H); ¹³C-NMR (100 MHz, DMSO) δ 108.3 (q, $J = 4.1$ Hz), 119.4 (q, $J = 4.1$ Hz), 123.3 (q, $J = 272.3$ Hz), 125.3, 135.6 (d, $J = 31.3$ Hz), 150.7, 159.0, 183.6.

tert-Butyl 3-(5-chloro-2-methoxyphenyl)-6-(trifluoromethyl)-3-hydroxy-2-oxoindoline-1-carboxylate

(27): To a stirred solution of **26** (4.5 g, 20.9 mmol) in THF (50 mL) was added sodium hydride (1.67 g, 60~72% in mineral oil) at 0 °C. After 1 h, the reaction mixture was cooled at -20 °C, and a solution of **22** (ca. 2 eq) was added under an atmosphere of N₂. The mixture was allowed to warm to room temperature and stirred until **26** was consumed. The reaction mixture was diluted with ether, and quenched with 1N HCl under ice-bath cooling. The separated organic layer was washed with water, and brine, and then dried with Na₂SO₄. The crude solid obtained after evaporation was triturated with CH₂Cl₂ to afford pure **27** (6.1 g, 81%).

¹H-NMR (400 MHz, DMSO) δ 3.41 (s, 3H), 6.90 (s, 1H), 6.93 (d, $J = 9.0$ Hz, 1H), 7.03-7.05 (m, 2H), 7.19 (d, $J = 7.8$ Hz, 1H), 7.35 (dd, $J = 2.6, 8.7$ Hz, 1H), 7.79 (d, $J = 2.6$ Hz, 1H), 10.67 (brs, 1H).

tert-Butyl 3-(5-chloro-2-methoxyphenyl)-6-(trifluoromethyl)-2-oxoindoline-1-carboxylate (28): A mixture of **27** (107 mg, 0.3 mmol), Et₃SiH (144 μ l, 0.9 mmol), and TFA (70 μ l, 0.9 mmol) was heated at 110-120 °C in a sealed tube for 2 days. Excess Et₃SiH, and TFA were evaporated, and the resulting residue was purified by flash chromatography (CH₂Cl₂ : MeOH = 97 : 3) to afford **28** (77.8 mg, 76 %).

¹H-NMR (400 MHz, DMSO) δ 3.57 (s, 3H), 4.92 (s, 1H), 7.02 (d, $J = 8.8$ Hz, 1H), 7.06-7.10 (m, 2H), 7.22 (d, $J = 7.1$ Hz, 1H), 7.34-7.37 (m, 2H), 10.79 (brs, 1H).

8-2) Preparation of racemic 7

Like the synthesis of **5**, selective introduction of the Boc group to **28** according to the conventional methods [(Boc)₂O-NaHCO₃, (Boc)₂O-DMAP, (Boc)₂O-NaH] was unsuccessful. After several experimentations, we found that the usage of EtMgBr as a base was effective (Scheme SI-7).

Scheme SI-7. Protection with the Boc group

tert-Butyl 3-(5-chloro-2-methoxyphenyl)-6-(trifluoromethyl)-2-oxindoline-1-carboxylate (7): **28** (240 mg, 0.7 mmol) was dissolved in THF (3.5 mL). To this solution was added 0.86 M EtMgBr (0.72 mL, 0.7 mmol), (Boc)₂O (168 mg, 0.77 mmol) at -40 °C, and then allowed to stir at room temperature for 3 h. The reaction mixture was diluted with ether, and then quenched with saturated aqueous NH₄Cl. The aqueous layer was extracted with ether, and the combined organic layers were washed with water and brine and then dried over Na₂SO₄. After the removal of solvent, purification by flash column chromatography (hexane : ethyl acetate = 9 : 1) was carried out to give racemic **7** in 80% yield (247 mg).

¹H-NMR (400 MHz, CDCl₃) δ 1.67 (s, 9H), 3.67 (s, 3H), 4.86 (s, 1H), 6.82 (d, *J* = 8.8 Hz, 1H), 7.12-7.14 (m, 2H), 7.27 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 8.20 (s, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.0, 48.7, 56.1, 85.0, 112.1 (q, *J* = 4.1 Hz), 112.8, 121.4 (q, *J* = 3.3 Hz), 123.9 (q, *J* = 271.4 Hz), 124.1, 126.1 (d, *J* = 53.5 Hz), 129.4, 130.8, 131.1, 131.3, 140.6, 149.1, 155.8, 173.2; FAB-MS (*m*NBA) *m/z* 441 (M)⁺; FAB-HRMS (*m*NBA) Calcd for C₂₁H₁₉ClF₃NO₄ (M)⁺ 471.0955. Found 471.0952.

8-3) Effects of solvent and temperature

The effects of basic parameters were summarized in Table SI-2. In contrast to **5b**, IPA was not suitable solvent for the reaction of **7**, resulting in lower enantioselectivity probably due to low solubility of the substrate (entry 1). Among the solvents tested, acetone gave the best result (entries 2-4). Thus, most of the reactions related to the BMS compound **3** and **6c** were carried out using acetone as a solvent. Notably, low temperature decreased enantioselectivity while higher temperature (50 °C) did not affect it significantly (entries 6, 8).

Table SI-2. Optimization of the reaction conditions

entry	solvent	temp.	time (h)	yield (%)	ee ^a (%)
1	IPA	rt	4	89	44
2	THF	rt	3	85	52
3	CH ₃ CN	rt	48	60	22
4	acetone	rt	3	76	65
5 ^b	acetone	rt	3	70	70
6 ^c	acetone	-40 °C ~ -20 °C	12	21	49
7	acetone	0 °C	18	90	71
8	acetone	50 °C	1.5	89	69
9 ^d	acetone	rt	2	86	23

^a Determined by chiral HPLC analysis. ^b The starting material was slowly added over 2 h.

^c **5h** was used in place of **7**. ^d[Pd((*S*)-binap)(μ -OH)]₂(TfO)₂ was used in place of **2**.

8-4) Catalytic asymmetric fluorination of **7**

The reaction was conducted according to the general procedure described above. Acetone was used as a solvent, and the reaction was carried out at 0 °C.

tert-Butyl 3-(5-chloro-2-methoxyphenyl)-3-fluoro-6-(trifluoromethyl)-2-oxoindoline-1-carboxylate (**8**):

¹H-NMR (400 MHz, CDCl₃) δ 1.67 (s, 9H), 3.54 (s, 3H), 6.76 (d, *J* = 8.8 Hz, 1H), 7.27 (d, *J* = 7.8 Hz, 1H), 7.34 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 2.4 Hz, 1H), 8.25 (s, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.0, 56.1, 85.4, 90.5 (d, *J* = 185.1 Hz), 112.6 (m), 112.8 (d, *J* = 1.6 Hz), 121.8 (m), 123.5 (q, *J* = 271.5 Hz), 125.3, 126.1 (d, *J* = 13.1 Hz), 126.4 (d, *J* = 28.0 Hz), 126.6 (d, *J* = 1.7 Hz), 128.7 (d, *J* = 18.9 Hz), 130.4, 133.5 (dq, *J* = 3.3, 32.1 Hz), 141.5 (d, *J* = 5.0 Hz), 148.7, 153.3 (d, *J* = 6.6 Hz), 169.0 (d, *J* = 20.6 Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -77.5, 13.2; FAB-MS (*m*NBA) *m/z* 460 (M+1)⁺; [α]_D²⁸ +103.5 (c = 1.17, CHCl₃) (69% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 200 / 1, 1.0 mL / min, 254 nm) *t*_r (major) = 7.8 min, *t*_r (minor) = 10.8 min; FAB-HRMS (*m*NBA) Calcd for C₂₁H₁₉O₄NF₄Cl (M+1)⁺ 460.0939. Found 460.0947; IR (solid) 2983, 2933, 1788, 1736, 1621, 1492, 1439, 1359, 1319, 1299, 1240, 1148, 1062, 1024, 968, 887, 842, 768, 647 cm⁻¹.

8-5) Enantioenrichment

3-(5-chloro-2-methoxyphenyl)-3-fluoro-6-(trifluoromethyl) indolin-2-one (3): **8** (124 mg, 0.268 mmol, 70% ee) was dissolved in CH₂Cl₂ (0.5 mL). To this solution was added TFA (124 μ l, 1.6 mmol) at room temperature, and the mixture was stirred at room temperature for 8 h. The reaction mixture was diluted with ethyl acetate, and then quenched with saturated aqueous NaHCO₃ under ice-bath cooling. The aqueous layer was extracted with ethyl acetate, and the combined organic layers were washed with water and brine, and then dried over Na₂SO₄. After the removal of solvent, purification by flash column chromatography (hexane : ethyl acetate = 4 : 1) was carried out to give **3** in 75% yield (72.4 mg). This product was found to be identical with the reported compound by comparison with ¹H-NMR.^{4a,5} The ee of the obtained BMS compound was determined to be 69% ee, indicating that substantially no racemization occurred during the deprotection.

¹H-NMR (400 MHz, CDCl₃) δ 3.55 (s, 3H), 6.78 (dd, *J* = 1.5, 8.8 Hz, 1H), 7.16 (s, 1H), 7.20 (dd, *J* = 2.0, 7.8 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.35 (dd, *J* = 2.7, 8.8 Hz, 1H), 7.80 (d, *J* = 1.0, 2.7 Hz, 1H), 8.92 (s, 1H); HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 90 / 10, 1.0 mL / min, 254 nm) *t*_r (major) = 7.5 min, *t*_r (minor) = 10.3 min; [α]_D²⁹ = +108.3 (c = 0.51, MeOH) (69% ee). {Lit.⁵ [α]_D²⁸ = +168 (c = 0.132, MeOH) (>99% ee, *S* enantiomer)}. By comparing the value of optical rotation with the reported value,⁵ the

⁵ Shibata, N.; Ishimaru, T.; Suzuki, E.; Kirk, K. L. *J. Org. Chem.* **2003**, *68*, 2494-2497.

absolute configuration of **8** was determined to be *S*.

As reported by Shibata et al, recrystallization (hexane/CH₂Cl₂) of the product **3** (69% ee) obtained by our method furnished the optically pure **3** in 57% yield. Interestingly, the second crop was found to be racemic.

9) Catalytic Enantioselective Monofluorination of **10**

9-1) Details of the optimization of the reaction conditions

When the reaction was carried out in THF, the monofluorinated product **11** was obtained in 29% yield with 21% ee, accompanying the difluorinated product **13** (y. 19%) (Table SI-3, entry 1). We speculated that fluorination occurred enantioselectively, but rapid racemization resulted in low enantioselectivity. As can be seen from entries 2-4, the enantioselectivity increased as the size of the alcoholic solvents became smaller, suggesting that smooth ring opening reaction with alcohol suppressed racemization of the monofluorinated compound **11**, affording the compound **12** with high enantioselectivity. It is likely that other results described in this table support this way of thinking. When the amount of MeOH was reduced, the product ratio between **12** : **14** became better (entries 5, 12). Unfortunately, however, the ee of **12** was also observed. In most cases, solvolysis of **10** to give **14** was a competitive reaction, which is a future task to be solved. Among the co-solvents examined, halogenated solvents were the best in terms of enantioselectivity. Slow addition of the substrate was also examined to suppress the undesired solvolysis of **10** (entry 13). But, a similar result was obtained.

(continued to the next page)

Table SI-3. Details of catalytic enantioselective monofluorination of 10

entry	solvent	product	12 : 14 ^a	time (h)	yield (%)	ee ^b (%)
1	THF	11	-	43	29 ^c	21
2	IPA	12 (R = <i>i</i> -Pr)	10 : 1	50	20	0
3	EtOH	12 (R = Et)	1.4 : 1	50	45	60
4	MeOH	12 (R = Me)	1 : 2.8	18	20	90
5	THF-MeOH (5:1)	12 (R = Me)	5.6 : 1	60	55	60
6	THF-MeOH (1:1)	12 (R = Me)	1.6 : 1	18	51	84
7	THF-EtOH (1:1)	12 (R = Me)	5.6 : 1	58	30	77
8	acetone-MeOH (1:1)	12 (R = Me)	1.7 : 1	26	43	89
9	CH ₂ Cl ₂ -MeOH (1:2)	12 (R = Me)	1 : 2.75	12	26	94
10	CH ₂ Cl ₂ -MeOH (1:1)	12 (R = Me)	1 : 1	16	46	92
11	ClCH ₂ CH ₂ Cl-MeOH (1:1)	12 (R = Me)	1.3 : 1	18	53	93
12	ClCH ₂ CH ₂ Cl-MeOH (2:1)	12 (R = Me)	1.4 : 1	36	51	88
13 ^d	ClCH ₂ CH ₂ Cl-MeOH (1:1)	12 (R = Me)	1.2 : 1	18	50	93
14	CHCl ₃ -MeOH (1:1)	12 (R = Me)	1 : 1.1	30	42	90

^a Determined by ¹H NMR of the crude products. ^b Determined by chiral HPLC analysis.

^c Difluorinated product **13** was isolated in 19% yield. ^d The starting material **10** was slowly added over 8.5 h.

9-2) Procedure for the catalytic enantioselective monofluorination of 10

The starting material **10** (56 mg, 0.24 mmol) and the Pd complex **2** (12 mg, 0.006 mmol) were dissolved in dichloroethane (0.24 mL) and MeOH (0.24 mL). To this solution was added NFSI (112 mg, 0.36 mmol) under ice-bath cooling. The resultant mixture was stirred at room temperature (20~23 °C) for 18 h. After the completion of the reaction (TLC: hexane-acetone system), saturated aqueous NaCl was added for quenching. Aqueous layer was extracted with ether (3 x 10 mL). The combined organic layers were washed with brine and dried over Na₂SO₄. After removal of the solvent, flash column chromatography (SiO₂, hexane : acetone = 10 : 1) afforded the desired product **12** (36 mg, 53%) and the by-product **14** (26.4 mg, 40%) as a colorless oil, respectively. The ee of the product **12** was determined by chiral HPLC analysis.

10: This compound was synthesized according the reported procedure. ²

11: ¹H-NMR (400 MHz, CDCl₃) δ 1.62 (s, 9H), 5.69 (d, *J* = 51.2 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.40-7.50

(m, 2H), 7.85 (d, $J = 8.23$ Hz, 1H); FAB-MS (*mNBA*) m/z 251 (M)⁺, 252 ($M+1$)⁺; HPLC (DAICEL CHIRALPAK AD-H, hexane / IPA = 99/1, 1.0 mL / min, 254 nm) t_r (minor) = 10.6 min, t_r (major) = 16.2 min.

Methyl 2-(2-*tert*-butoxycarbonylamino-phenyl)-2-fluor *o*-acetate (12): ¹H-NMR (400 MHz, CDCl₃) δ 1.53 (s, 9H), 3.80 (s, 3H), 5.91 (d, $J = 46.0$ Hz, 1H), 7.13 (t, $J = 7.6$ Hz, 1H), 7.25 (brs, 1H), 7.34-7.42 (m, 2H), 7.89 (d, $J = 8.1$ Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.3, 53.0, 80.7, 88.0 (d, $J = 186$ Hz), 123.2, 124.0, 127.9 (d, $J = 7.4$ Hz), 130.4, 130.5, 136.5 (d, $J = 2.5$ Hz), 153.0, 169.1 (d, $J = 27.1$ Hz); ¹⁹F-NMR (376 MHz, CDCl₃) δ -107.1 (d, $J = 46.0$ Hz); FAB-MS (*mNBA*) m/z 297 (M)⁺, 298 ($M+1$)⁺, 242 ($M+2H-tBu$)⁺; $[\alpha]_D^{27}$ -82.2 ($c = 1.05$, CHCl₃) (90% ee); HPLC (DAICEL CHIRALCEL OD-H, hexane / IPA = 95 / 5, 1.0 mL / min, 254 nm) t_r (major) = 6.1 min, t_r (minor) = 7.3 min; IR (neat) 3428, 2978, 1727, 1592, 1515, 1451, 1367, 1299, 1231, 1151, 1042, 1021, 752 cm⁻¹; Anal. Calcd for C₁₄H₁₈FNO₄: C, 59.35. H, 6.40. N, 4.94. Found: C, 59.28. H, 6.34. N, 4.90.

13: ¹H-NMR (400 MHz, CDCl₃) δ 1.62 (s, 9H), 7.28 (t, $J = 8.0$ Hz, 1H), 7.51-7.60 (m, 2H), 7.90-7.98 (m, 1H); FAB-MS (*mNBA*) m/z 269 (M)⁺, 270 ($M+1$)⁺.

14: ¹H-NMR (400 MHz, CDCl₃) δ 1.53 (s, 9H), 3.64 (s, 2H), 3.72 (s, 3H), 7.05 (dt, $J = 1.2, 7.6$ Hz, 1H), 7.18 (dd, $J = 1.4, 7.6$ Hz, 1H), 7.25-7.30 (m, 1H), 7.60 (brs, 1H), 7.77 (d, $J = 8.0$ Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 28.3, 38.4, 52.5, 80.3, 123.6, 124.2, 125.1, 128.3, 130.6, 137.1, 153.5, 172.6; FAB-MS (*mNBA*) m/z 265 (M)⁺, 210 ($M+2H-tBu$)⁺.

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¹H NMR

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