SUPPORTING INFORMATION

General Procedure for the Synthesis of α-Methyl β-(Fluoroalkyl) β-Enamino Esters 3. *n*-Butyllithium (2.5 M in hexanes, 6.4 mL, 16.0 mmol) was added dropwise to a stirred solution of diisopropylamine (2.24 mL, 16.8 mmol) in THF (10 mL) at -30 °C. After stirring the reaction mixture for 30 min, the solution was cooled to -50 °C and methyl propionate **2** (0.91 mL, 8.0 mmol) in THF (10 mL) was added. The resulting mixture was stirred at -50 °C for 1.5 h and cooled to -78 °C. Then, a solution of the appropriate imidoyl chloride **1** (8.0 mmol.) in THF (10 mL) was slowly added. The reaction mixture was monitored by means of TLC analysis. After total disappearance of the starting material (TLC), the solvents were removed under reduced pressure. The reaction was quenched with saturated ammonium chloride solution and extracted with methylene chloride (2 x 25 mL). The combined organic layers were dried over sodium sulfate. Filtration and evaporation furnished the crude products **3**, which were purified by means of *flash* silica gel column chromatography as indicated.

Methyl 4,4,4-trifluoro-3-(4-methoxyanilino)-2-methyl-2-butenoate (3a). *Flash* chromatography (*n*-hexane-EtOAc (8:1)) on silica gel (R_f=0.43) gave a yellow oil (92%): ^{1}H NMR (250 MHz) (*Z*-enamino tautomer) 1.21 (q, $^5J_{HF}$=1.2, 3H), 2.93 (s, 3H), 2.98 (s, 3H), 5.98 (d, *J*=8.9, 2H), 6.09 (d, *J*=8.9, 2H), 8.6 (br s, 1H); (imino tautomer) 0.60 (d, *J*=7.3, 3H); 2.93 (s, 3H), 2.98 (s, 3H), 3.08 (q, *J*=7.3, 1H), 5.90 (d, *J*=8.9, 2H), 6.09 (d, *J*=8.9, 2H); ^{13}C NMR (62.8 MHz) (Z-enamino tautomer) 12.9 (q), 51.9 (q), 55.3 (q), 88.9 (q, $^3J_{CF}$=5.7), 114.1 (d), 120.4 (q, $^1J_{CF}$=277.0), 126.7 (d), 127.8 (s), 135.3 (s), 156.5 (q, $^2J_{CF}$=24.7), 169.8 (s); (imino tautomer) 13.2 (q), 39.3 (d), 52.7 (q), 55.3 (q), 114.4 (d), 119.9 (q, $^1J_{CF}$=278.2), 119.9 (d), 139.8 (s), 157.4 (s), 157.6 (q, $^2J_{CF}$=24.7), 169.8 (s). ^{19}F NMR (235 MHz) (Z-enamino tautomer) -58.6 (s), (imino tautomer) -68.1 (s). HRMS calc. for $C_{13}H_{14}F_3NO_3$ 289.0925, found 289.0915.

Ethyl 4,4,4-trifluoro-3-(4-methoxyanilino)-2-methyl-2-butenoate (3b). *Flash* chromatography (*n*-hexane-EtOAc (7:1)) on silica gel (R_f=0.45) gave a yellow oil (87%): ^{1}H NMR (400 MHz) (Z-enamino tautomer) 1.21 (t, *J*=3.52, 3H), 1.96 (q, $^5J_{HF}$=2.0, 3H), 3.68 (s, 3H), 4.10 (q, *J*=3.5, 2H), 6.73 (d, *J*=9.0, 2H), 6.82 (d, *J*=9.0, 2H), 9.31 (br s, 1H); (imino tautomer) 1.19 (t, *J*=7.0, 3H), 1.29 (d, *J*=7.0, 3H), 3.71 (s, 3H), 3.81 (q, *J*=7.5, 1H), 4.14 (q, *J*=7.0, 2H), 6.72 (d, *J*=8.5, 2H), 6.83 (d, *J*=9.0, 2H); ^{13}C NMR (100 MHz) (Z-enamino tautomer) 12.9 (q), 14.0 (q), 55.3 (q), 60.9 (t), 107.6 (q, $^3J_{CF}$=1.9), 113.9 (d), 121.8 (q, $^1J_{CF}$=265.8), 123.2 (d), 135.5 (s), 142.7 (q, $^2J_{CF}$=29.9), 156.5 (s) 170.0 (s); (imino tautomer) 13.0 (q), 13.8 (q), 39.5 (d), 55.3 (q), 61.8 (t), 114.4 (d), 119.4 (q, $^1J_{CF}$=279.1), 119.9 (d), 139.9 (s), 157.4 (s),

157.9 (q, $^2J_{CF}$=31.8), 169.2 (s). ^{19}F NMR (376 MHz) (Z-enamino tautomer) -58.9 (s), (imino tautomer) -68.1 (s). HRMS calc. for $C_{14}H_{16}F_3NO_3$ 303.1082, found 303.1088.

***tert*-Butyl 4,4,4-trifluoro-3-(4-methoxyanilino)-2-methyl-2-butenoate (3c).** *Flash* chromatography (*n*-hexane-EtOAc (15:1)) on silica gel (R_f=0.6) gave a yellow oil (91%): ^{1}H NMR (250 MHz) (Z-enamino tautomer) 1.40 (s, 9H), 1.92 (q, $^5J_{HF}$=1.8, 3H), 3.69 (s, 3H), 6.73 (d, *J*=8.6, 2H), 6.82 (d, *J*=8.8 Hz, 2H), 9.14 (br s, 1H); (imino tautomer) 1.20 (d, *J*=7.3, 1H); 1.35 (s, 9H), 3.68 (m, 1H), 3.70 (s, 3H), 6.73 (d, *J*=8.6, 2H), 6.82 (d, *J*=8.8, 2H); ^{13}C NMR (100 MHz) (Z-enamino tautomer) 12.9 (q), 27.7 (q), 40.4 (q) 55.3 (q), 82.6 (s), 114.5 (d), 119.5 (q, $^1J_{CF}$=279.1), 119.9 (d), 140.2 (s), 157.3 (s), 158.7 (q, $^2J_{CF}$=31.8), 168.2 (s); (imino tautomer) 12.9 (q), 27.7 (q), 40.4 (d), 55.4 (q), 82.7 (s), 114.5 (d), 119.5 (q, $^1J_{CF}$=280.2), 140.2 (s), 157.3 (s), 158.7 (q, $^2J_{CF}$=31.7), 168.2 (s); ^{19}F NMR (235 MHz) (Z-enamino tautomer) -58.8 (s), (imino tautomer) -67.5 (s). HRMS calc. for $C_{16}H_{20}F_3NO_3$ 331.1395, found 331.1394.

Methyl 4-chloro-4,4-difluoro-3-(4-methoxyanilino)-2-methyl-2-butenoate (3d). *Flash* chromatography (*n*-hexane-EtOAc (8:1)) on silica gel (R_f=0.5) gave a yellow oil (72%): ^{1}H NMR (400 MHz) (Z-enamino tautomer), 2.01 (q, $^5J_{HF}$=2.5, 3H), 3.60 (s, 3H), 3.68 (s, 3H), 6.69 (d, *J*=5.5, 2H), 6.82 (d, *J*=6.5, 2H), 8.89 (br s, 1H); (imino tautomer) 1.36 (d, *J*=7.5, 3H); 3.63 (s, 3H), 3.70 (s, 3H), 3.84 (q, *J*=7.2, 1H), 6.69 (d, *J*=5.5, 2H), 6.82 (d, *J*=6.5, 2H); ^{13}C NMR (100 MHz) (Z-enamino tautomer) 17.2 (q), 51.8 (q), 52.1 (q), 106.77 (s), 114.5 (d), 119.8 (d), 120.4 (t, $^1J_{CF}$=277.0), 139.2 (s), 146.7 (t, $^2J_{CF}$=24.1), 157.3 (s), 169.8 (s); (imino tautomer) 13.8 (q), 39.6 (d), 52.5 (q), 55.3 (q), 114.0 (d), 119.3 (d), 123.5 (t, $^1J_{CF}$=277.0), 134.2 (t, $^2J_{CF}$=24.1), 135.3(s) 156.4 (s), 169.0 (s); ^{19}F NMR (376 MHz) (Z-enamino tautomer) -48.7 (s); (imino tautomer) -55.7 (d, J_{FF}=167.2), -56.9 (d, J_{FF}=167.2). HRMS (FAB) calc. for (M^++1) $C_{13}H_{15}ClF_2NO_3$ 306.0708, found 306.0696.

Methyl 4,4,5,5,5-trifluoro-3-(4-methoxyphenilimino)-2-methylpentanoate (3e). *Flash* chromatography (*n*-hexane-EtOAc (8:1)) on silica gel (R_f=0.6) gave a yellow oil (71%): ^{1}H NMR (400 MHz) (imino tautomer) 1.3 (d, *J*=7.0, 3H); 3.65 (s, 3H), 3.72 (s, 3H), 3.87 (q, *J*=7.5, 1H), 6.69 (d, *J*=8.5, 2H), 6.83 (d, *J*=8.5, 2H); ^{13}C NMR (100 MHz) (imino tautomer) 13.7 (q), 40.3 (d), 53.0 (q), 55.8 (q), 109.3 (qt, $^1J_{CF}$=294.6, $^2J_{CF}$=37.6), 114.9 (d), 117.3 (tq, $^1J_{CF}$=312.9, $^2J_{CF}$=35.7), 120.2 (d), 140.4 (s), 157.9 (s), 159.4 (t, $^2J_{CF}$=27.0), 170.2 (s); ^{19}F NMR (376 MHz) (imino tautomer) -81.67 (s), -113.41 (q, J_{FF}=308.9). HRMS calc. for $C_{14}H_{14}F_5NO_3$ 339.0893, found 339.0906.

General Procedure for the Synthesis of α-Methyl β-(Fluoroalkyl) β-Amino Esters 4. To a solution of anhydrous zinc iodide (1.91 g, 6.0 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C was added the corresponding α-methyl β-(fluoroalkyl) β-enamino ester **3** (2.0 mmol). The resulting mixture was stirred at the same temperature for 1 h and then $NaBH_4$ (0.375 g, 10 mmol) was added, also at 0 °C. The solution was allowed to reach room temperature, and then monitored by means of TLC. The reaction was quenched with saturated ammonium chloride solution and extracted with dichloromethane (3 × 20 mL). The organic layers were combined, washed with brine and dried over sodium sulfate. After filtration, the solvents were removed under reduced pressure to provide the crude reaction mixture consisting of **4** and/or **5**. Purification was carried out as indicated in each case.

Methyl 4,4,4-trifluoro-3-(4-methoxyanilino)-2-methylbutanoate (4a). (2*R,3*R**)-4a.** *Flash* chromatography (*n*-hexane-EtOAc (7:1)) on silica gel (R_f=0.4) gave a yellow solid (81%): mp 64-6 °C. ^{1}H NMR (250 MHz) 1.23 (d, *J*=7.1, 3H), 2.88 (m, 1H), 3.45 (br d, *J*=11.1, 1H), 3.58 (s, 3H), 3.67 (s, 3H), 4.31-4.41 (m, 1H), 6.63 (d, *J*=8.8, 2H), 6.70 (d, *J*=9.0, 2H); ^{13}C NMR (62.8 MHz) 11.5 (q), 39.6 (d), 52.2 (q), 55.6 (q), 58.4 (q, $^2J_{CF}$=28.1), 114.7 (d), 115.8 (d), 122.3 (q, $^1J_{CF}$=282.5), 139.9 (s), 153.3 (s), 173.2 (s); ^{19}F NMR (235 MHz) -73.4 (d, J_{FH}=7.3). HRMS calc. for $C_{13}H_{16}F_3NO_3$ 291.1082, found 291.1079. Anal. Calcd for $C_{13}H_{16}F_3NO_3$: C, 53.61; H, 5.54; N, 4.81. Found: C, 53.66; H, 5.52; N, 4.80. **(2*S**,3*R**)-4a.** Obtained and purified from the crude mixture in the reduction reaction of **3a** with $NaBH_3CN$. *Flash* chromatography (*n*-hexane-EtOAc (7:1)) on silica gel (R_f=0.5) gave a yellow oil (17%): ^{1}H NMR (250 MHz) 1.22 (d, *J*=7.1, 3H); 2.87-2.96 (m, 1H), 3.63 (s, 3H), 3.66 (s, 3H), 3.84-3.92 (m, 1H), 4.37 (br d, *J*=9.8, 1H), 6.59 (d, *J*=9.0, 2H), 6.72 (d, *J*=9.8, 2H); ^{13}C NMR (62.8 MHz) 14.7 (q), 38.7 (d), 52.1 (q), 55.6 (q), 59.64 (q, $^2J_{CF}$=28.9), 114.8 (d), 114.9 (d), 125.5 (q, $^1J_{CF}$=282.5), 140.5 (s), 152.9 (s), 174.2 (s); ^{19}F NMR (235 MHz) -73.8 (d, J_{FH}=7.3). HRMS calc. for $C_{13}H_{16}F_3NO_3$ 291.1082, found 291.1087.

Ethyl (2*R,3*R**)-4,4,4-trifluoro-3-(4-methoxyanilino)-2-methylbutanoate (4b).** *Flash* chromatography (*n*-hexane-EtOAc (7:1)) on silica gel (R_f=0.3) gave a yellow solid (81%): mp 40-2 °C. ^{1}H NMR (400 MHz) 1.09 (t, *J*=8.7, 3H), 1.20 (d, *J*=4.4, 3H); 2.84 (m, 1H), 3.51 (br d, *J*=6.5, 1H), 3.64 (s, 3H), 3.40 (q, *J*=4.4, 2H), 4.30-4.40 (m, 1H), 6.60 (d, *J*=5.7 , 2H), 6.68 (d, *J*=5.6, 2H); ^{13}C NMR (100 MHz) 11.4 (q), 13.8 (q), 39.6 (d), 55.5 (q), 58.2 (q, $^2J_{CF}$=28.1), 61.1 (t), 114.7 (d), 115.6 (d), 125.7 (q, $^1J_{CF}$=283.0), 140.0 (s), 153.2 (s), 172.7 (s); ^{19}F RMN (376 MHz) -73.5 (d, J_{FH}=8.0). HRMS calc. for $C_{13}H_{18}F_3NO_3$ 305.1238, found 305.1251.

Anal. Calcd for $C_{13}H_{18}F_3NO_3$: C, 55.08; H, 5.94; N, 4.59. Found: C, 55.10; H, 5.96; N, 4.57.

***tert*-Butyl (2*R**,3*R**)-4,4,4-trifluoro-3-(4-methoxyanilino)-2-methylbutanoate (4c).** *Flash* chromatography (*n*-hexane-$CHCl_3$-EtOAc (10:2:1)) on silica gel (R_f=0.3) gave a yellow solid (70%): mp 86-8 °C. ^{1}H NMR (400 MHz) 1.18 (d, *J*=7.2, 3H), 1.29 (s, 9H); 2.78 (m, 1H), 3.52 (br d, *J*=10.5, 1H), 3.67 (s, 3H), 4.28-4.37 (m, 1H), 6.61 (d, *J*=6.7, 2H), 6.70 (d, *J*=6.7, 2H); ^{13}C NMR (100 MHz) 11.5 (q), 27.7 (q), 40.5 (d), 55.6 (q), 58.0 (q, $^2J_{CF}$=28.0), 81.6 (s), 114.7 (d), 115.3 (d), 125.8 (q, $^1J_{CF}$=282.0), 140.2 (s), 153.1 (s), 171.8 (s); ^{19}F RMN (376 MHz) -73.2 (d, J_{FH}=7.4). HRMS calc. for $C_{16}H_{22}F_3NO_3$ 333.1551, found 333.1559. Anal. Calcd for $C_{16}H_{22}F_3NO_3$: C, 57.65; H, 6.65; N, 4.20. Found: C, 55.60; H, 6.62; N, 4.23.

Methyl (2*R,3*R**)-4-chloro-4,4-difluoro-3-(4-methoxyanilino)-2-methyl-2-butanoate (4d).** *Flash* chromatography (*n*-hexane-EtOAc (8:1)) on silica gel (R_f=0.15) gave a yellow solid (80%): mp 42-5 °C; ^{1}H NMR (400 MHz) 1.22 (d, *J*=7.0, 3H); 2.93-3.00 (m, 1H), 3.51 (br. d, *J*=11.0, 1H), 3.57 (s, 3H), 3.66 (s, 3H), 4.41-4.50 (m, 1H), 6.63 (d, *J*=9.0, 2H), 6.70 (d, *J*=9.0, 2H); ^{13}C NMR (100 MHz) 11.9 (q), 40.5 (d), 55.2 (q), 55.6 (q), 63.5 (q, $^2J_{CF}$=24.1), 114.7 (d), 115.5 (d), 130.2 (q, $^1J_{CF}$=297.5), 140.1 (s), 153.2 (s), 173.5 (s); ^{19}F NMR (376 MHz) -59.6 (dd, J_{FF}=168.4, J_{FH}=9.1), -58.0 (dd, J_{FF}=163.8, J_{FH}=9.1). HRMS calc. for $C_{13}H_{16}ClF_2NO_3$ 307.0786, found 307.0798. Anal. Calcd for $C_{13}H_{16}ClF_2NO_3$: C, 50.73; H, 5.20; N, 4.55. Found: C, 50.87; H, 5.14; N, 4.67.

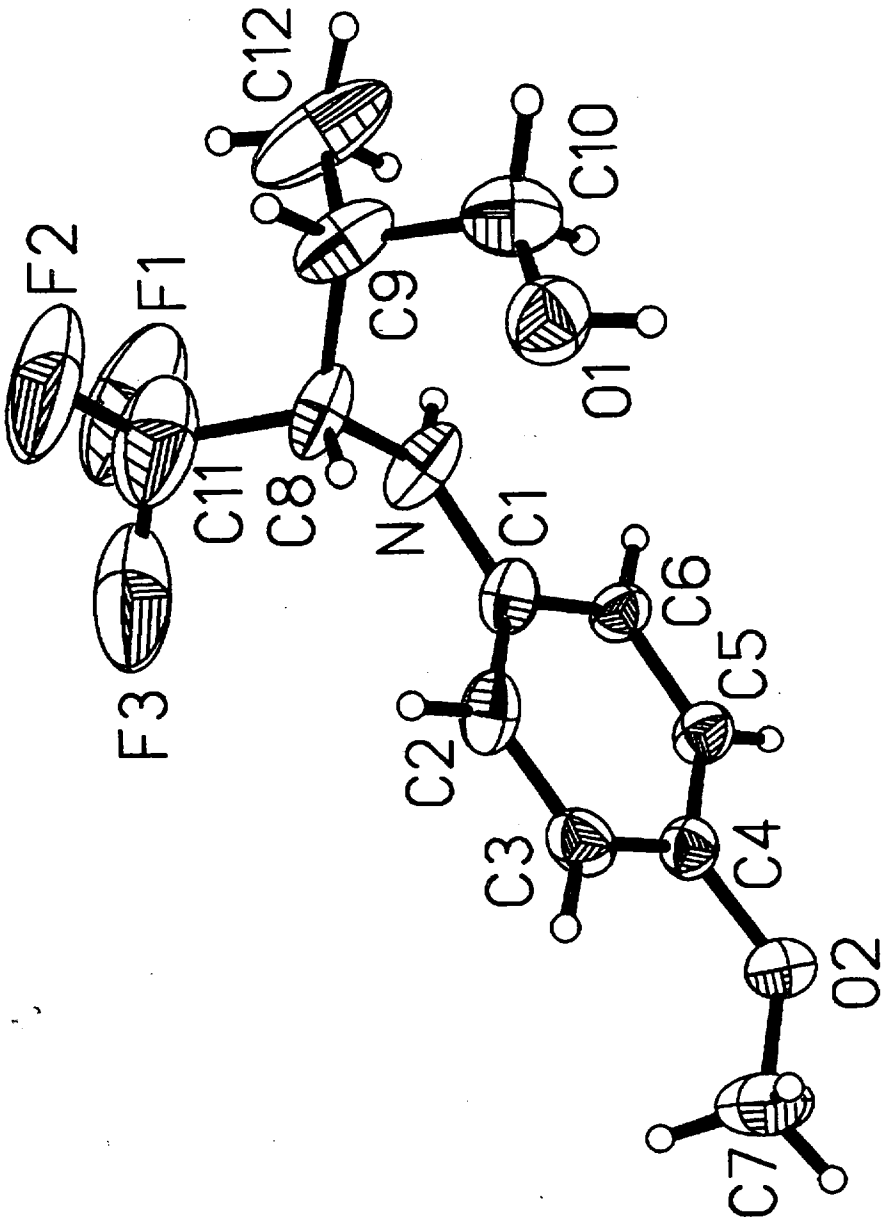
Methyl (2*R,3*R**)-4,4,5,5,5-pentafluoro-3-(4-methoxyanilino)-2-methylpentanoate (4e).** *Flash* chromatography ($CHCl_3$-*n*-hexane (5:1)) on silica gel (R_f=0.17) gave a pale yellow solid (30%): mp 86-8 °C; ^{1}H NMR (250 MHz) 1.20 (d, *J*=7.2, 3H); 2.89-2.94 (m, 1H), 3.44 (br. d, *J*=11.3, 1H), 3.50 (s, 3H), 3.65 (s, 3H), 4.47-4.62 (m, 1H), 6.56 (d, *J*=12.3, 2H), 6.70 (d, *J*=12.3, 2H); ^{13}C NMR (62.8 Mhz) 11.6 (q), 39.2 (d), 55.1 (d), 55.5 (q), 55.6 (t, $^2J_{CF}$=24.8), 114.7 (d), 115.1 (d), 110.0-122.0 (C_2F_5 signals are obscured due to their low intensity) 139.3 (s), 153.0 (s), 173.3 (s); ^{19}F NMR (250 MHz) -82.1 (s), -117.6 (dd, J_{FF}=274.2, J_{FH}=4.7), -126.8 (dd, J_{FF}=274.2, J_{FH}=22.3). HRMS calc. for $C_{14}H_{16}F_5NO_3$ 341.1050, found 341.1051. Anal. Calcd for $C_{14}H_{16}F_5NO_3$: C, 49.27; H, 4.73; N, 4.10. Found: C, 49.33; H, 4.76; N, 4.04.

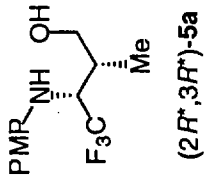
Synthesis of (2*R,3*R**)-4,4,4-Trifluoro-3-(4-methoxyanilino)-2-methyl-1-butanol (5a).** $LiAlH_4$ (69 mg, 1.8 mmol) was added to a solution of β-amino ester **4a** (177 mg, 0.6 mmol) in THF (12 mL) at -50 °C. The resulting mixture was stirred for 2h at -50 °C under argon atmosphere. The reaction was quenched with

saturated ammonium chloride solution. A similar reaction work-up to that described in the synthesis of α-methyl-β-fluoroalkyl-β-amino esters **4** yielded crude **5a** as a brown solid. The product was purified by means of *flash* chromatography (*n*-hexane-EtOAc (2:1)) on silica gel (R_f=0.5) (95%): mp 63-5°C; ^{1}H NMR (250 MHz) 0.92 (d, *J*=7.5 Hz, 3H); 1.62 (br s, 1H), 2.20 (m, 1H), 3.40-3.57 (m, 3H), 3.68 (s, 3H), 4.21 (br s, 1H), 6.66 (d, *J*=9.2, 2H), 6.71 (d, *J*=9.2, 2H); ^{13}C NMR (62.8 MHz) 10.2 (q), 35.0 (d), 55.6 (q), 56.2 (q, $^2J_{CF}$=27.0), 64.5 (t), 114.8 (d), 115.4 (d), 126.6 (q, $^1J_{CF}$=283.3), 140.8 (s), 153.0 (s); ^{19}F NMR (235 MHz) -72.4 (d, $J_{F\text{-}H}$=8.2). HRMS calc. for $C_{12}H_{16}F_3NO_2$ 263.1133, found 263.1121. Anal. Calcd for $C_{12}H_{16}F_3NO_2$: C, 54.75; H, 6.13; N, 5.31. Found: C, 54.80; H, 6.16; N, 5.41.

(2*R,3*R**)-4,4,5,5,5-Pentafluoro-3-(4-methoxyanilino)-2-methyl-1-pentanol (5e).** This compound was obtained from the crude mixture in the reduction reaction of **4e** with ZnI_2/$NaBH_4$. Purification by means of *flash* chromatography ($CHCl_3$-*n*-hexane (5:1)) on silica gel (R_f=0.2) gave a brown solid (15%): mp 68-70 °C; ^{1}H NMR (400 MHz) 0.71-78 (m, 1H); 0.86 (d, *J*=6.8, 3H), 1.43 (br. s, 1H), 2.21 (br s, 1H), 2.30-3.47 (m, 2H), 3.62 (s, 3H), 4.35 (m, 1H), 6.58 (d, *J*=9.0, 2H), 6.66 (d, *J*=9.0, 2H); ^{13}C NMR (62.8 MHz) 10.2 (q), 35.2 (d), 53.0 (t, $^2J_{CF}$=20.3), 55.6 (q), 64.3 (t), 114.6 (d), 114.9 (d), 115.0-126.0 (C_2F_5 signals are obscured due to their low intensity), 140.8 (s), 152.7 (s); ^{19}F NMR (235 MHz) -82.4 (s), -119.4 (dd, J_{FF}=272.8, J_{FH}=8.2), -123.4 (dd, J_{FF}=273.0, J_{FH}=21.3). HRMS calc. for $C_{13}H_{16}F_5NO_2$ 313.1101, found 313.1103. Anal. Calcd for $C_{12}H_{16}F_3NO_2$: C, 54.75; H, 6.13; N, 5.31. Found: C, 54.70; H, 6.16; N, 5.33.

Synthesis of Ethyl (2*R,3*R**)-3-amino-4,4,4-trifluoro-2-methyl butanotate.** A solution of ceric ammonium nitrate (CAN) (2.74 g, 5 mmol) in water (4 mL) at 0 °C was added to a solution of **4b** (0.29 g, 1 mmol) in acetonitrile (8 mL). The reaction mixture was stirred at 0 °C until TLC showed no starting material (2 h). The aqueous phase was extracted with ethyl acetate (5 x 20 mL). The organic phases were pooled together, washed in sequence with Na_2SO_3 20% and $NaHCO_3$ 5% aqueous solutions and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. This yielded a crude brown oil (0.19 g, 90%): ^{1}H NMR (400 MHz) 1.18 (d, *J*=7.5, 3H), 1.20 (t, *J*=7.5, 3H); 1.53 (br s, 1H), 2.72-2.78 (m, 1H), 3.64-3.71 (m, 1H), 4.11 (q, *J*=7.5, 2H); ^{13}C NMR (100 MHz) 10.7 (q), 14.0 (q), 39.4 (d), 55.4 (q, $^2J_{CF}$=28.9), 61.1 (t), 126.1 (q, $^1J_{CF}$=280.1), 173.4 (s); ^{19}F NMR (376 MHz) -76.1 (d, J_{FH}=8.0). To date we have not been able to obtain satisfactory elemental analyses or HRMS (EI, FAB) for this compound because of its relatively fast decomposition, even at room temperature.





(2*R**,3*R**)-**5a**