# Efficient Syntheses of Fluorinated Aryl Alcohols of High Enantiomeric Purity via Boronic Esters

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## Introduction

The asymmetric synthesis of chiral fluoroorganic compounds has played an important role in the development of medicines and materials due to the influence of fluorine's unique properties.[1] Chiral fluorinated alcohols are versatile intermediates for the synthesis of antiferroelectric liquid crystalline molecules.[2] Recently, we have reported the synthesis of various kinds of trifluoromethylated alcohols as racemates.[3] There are some methods reported to make various kinds of fluorinated chiral alcohols but it was found to be very difficult to achieve a % enantiomeric excess close to 100.[4] Boron-based asymmetric reduction of ring-fluorinated acetophenone with $\beta$-chlorodiisopinocampheylborane (Aldrich: DIP-chloride™) has been recently reported.[4] Pentafluoroacetophenone reacted with DIP-chloride to produce the corresponding alcohol in 44% ee. The reason for low % ee may be due to a possible interaction between the pentafluorophenyl group and the chlorine atom of the reagent. Using the same reagent, 2,6-difluoroacetophenone was reduced to the corresponding alcohol in 74% ee. The best %ee obtained by using the DIP-chloride is 96% for 1-(4-fluorophenyl)ethanol and 1-[4-(trifluoromethylphenyl)ethanol. As we have shown earlier,[4] distereoselections in the 1000:1 range can be achieved by the use of a chiral director that has $C_2$ symmetry.[5] We have also shown that it is possible to cleave the chiral director [(*R*)-(*R**,*R**)]-1,2-dicyclohexyl-1,2-ethanediol from boron recovering in >90% yield.[6] In this work, we report a highly stereocontrolled boronic ester chemistry to make several fluorinated alryl alcohols in good isolated yields and in >99% enantiomeric excess.

## Results and Discussion

Homologation of simple alkyl or aryl boronic esters with different kinds of chiral directors is well documented in the literature.[7] Insertion of a carbon into the boron−carbon bond is accomplished by using a variety of lithio derivatives. To insert a >CHCl or a >CHBr group, low temperature generation of $LiCHCl_2$ or $LiCHBr_2$ is necessary; to insert a $CH_2$ group requires the low temperature generation of $LiCH_2Cl$. It is also well known that using a chiral director, it is possible to insert a chiral >CHCl or >CHBr group with >99% ee. Utilization of this methodology has led to much interesting chemistry.[7] We have applied this methodology to make several chiral fluorinated aryl alcohols in good yields and in >99% ee.

**1a** was obtained by the reaction of benzyl methyl borate and [(*R*)-(*R**,*R**)]-1,2-dicyclohexyl-1,2-ethanediol in ether and was homologated with (dichloromethyl)lithium to prepare [2(1*S*),4*R*,5*R*]-4,5-dicyclohexyl-2-(1-chloro-2-phenylethel)-1,3,2-dioxoborolane (**2a**).[8] [4*R*-(4α,5*β*)]-4,5-Dicyclohexyl-2-methyl-1,3,2-dioxoborolane **(1b)** was prepared from [(*R*)-(*R**,*R**)]-1,2-dicyclohexyl-1,2-ethanediol and trimethylboroxine by the literature method.[9] **1b** was homologated in a similar way using (dichloromethyl)-lithium to prepare [4*R*-[2(*S**),4α,5*β*]]-4,5-dicyclohexyl-2-methyl-1,3,2-dioxoborolane (**2b**).[10,11] Initially, we tried unsuccessfully to replace the α-chloro substituents with perfluoroalkyl groups by using Grignard reagents and lithium derivatives of perfluoroalkyl iodide. Grignard reagents and lithium derivatives were generated at two different temperatures, −100 and −78 °C; however no reaction was occurred. This may be due to the instability of the Grignard and lithio derivatives. It has been found that the replacement of chlorine in α-chloro boronic esters with different kinds of stable fluorinated aryl Grignard reagents is possible.[12] Thus, the reaction of **2a,b** with $R_fMgBr$ was carried out at −78 °C which gave **3c**−**j** in >89% yield (Scheme 1). Deboronation[10] of **3c**−**j** was carried out with sodium hydroxide/hydrogen peroxide in

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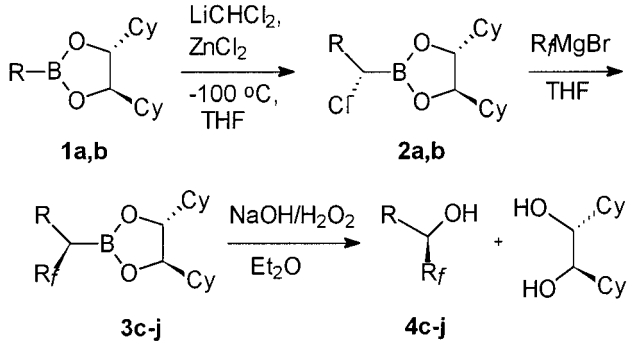
**Scheme 1**




**a**: R = Bn; **b**: R = Me; **c**: R = Bn, R *f* = $C_6F_5$;
**d**: R = Bn, R *f* = 4-$FC_6H_4$; **e**: R = Bn, R *f* = 4-$CF_3C_6H_4$;
**f**: R = Bn, R *f* = 3,5-$(CF_3)_2C_6H_3$; **g**: R = Me, R *f* = $C_6F_5$
**h**: R = Me, R *f* = 4-$FC_6H_4$; **i**: R = Me, R *f* = 4-$CF_3C_6H_4$
**j**: R = Me, R *f* = 3,5-$(CF_3)_2C_6H_3$;

diethyl ether which gave chiral fluorinated aryl alcohols **(4c−j)** in >79% yield (Scheme 1). The % ee of alcohols was determined by spectral measurement in the presence of Eu(hfc).[13]

All α-fluorinated boronic esters and chiral alcohols were characterized by IR, NMR and MS analyses. **3c** was crystallized from an ether/pentane mixture and its structure was determined by single crystal X-ray analyses. Compound **3c** crystallizes as monoclinic *P*2(1) with one molecule in the asymmetric unit. The absolute configuration cannot be determined reliably as only light atoms are present. The five membered borate ring is planar. The representation shown has C(1), C(15), and C(22) in the *R* configuration.

In summary, we have found a very efficient method to prepare chiral fluorinated aryl alcohols in good yield and in >99% enantiomeric excess using boronic ester chemistry.

## Experimental Section

**General Methods.** The usual procedures for handling reactive organometallic reagents were followed, including the use of an inert atmosphere (nitrogen) and THF (tetrahydrofuran) that had been rigorously dried over sodium benzophenone ketyl. **1a,**[8] **1b**[9] **2a,**[10,11] and fluorinated aryl magnesium bromide[12] were prepared by literature procedures. $^1$H, $^{13}$C, and $^{19}$F NMR spectra were recorded in $CDCl_3$ on a spectrometer operating at 200, 50, and 188 MHz, respectively. Chemical shifts are reported in ppm relative to the appropriate standard, $CFCl_3$ for $^{19}$F and tetramethylsilane/$CHCl_3$ for $^1$H and $^{13}$C NMR spectra. IR spectra were recorded using NaCl plates for neat liquids and KBr pellets for solids. Mass spectra were measured on an electron impact 70 ev spectrometer and high-resolution mass spectra (HRMS) were obtained using a suitable mass spectrometer. Elemental analyses were performed by Desert Analytics Laboratory, Tucson, AZ.

**General Procedure for the Synthesis of Fluorinated Arylmagnesium Bromide.**[12] To a suspension of magnesium turnings (1 g, 42.5 mmol) in THF (100 mL), a suitable fluorinated aryl bromide (40 mmol) was added very slowly at 0 °C. The bath was allowed to rise to room temperature and the solution was stirred for 3 h. The concentration of the Grignard reagent was determined by titration with 2-propanol in THF using 1,10-phenanthroline as an indicator.

**General Procedure for the Synthesis of α-Fluorinated Arylboronic Esters.** In a typical reaction, α-chloroboronic ester (**2a**,**b**) (10 mmol) was dissolved in THF (30 mL) and cooled to −78 °C. A solution of Grignard reagent was added dropwise with vigorous stirring. The bath temperature was allowed to rise to room temperature and was stirred overnight. Solvent was removed at reduced pressure and diethyl ether (50 mL) was added. It was washed with ammonium chloride solution and the ether phase was dried over anhydrous magnesium sulfate and filtered. Removal of solvent at reduced pressure yielded α-fluorinated aryl boronic esters **(3c−j)** in > 89% yield.

**[2(1′*R*),4*R*,5*R*]-4,5-Dicyclohexyl-2-[1-(pentafluorophenyl)-2-phenylethyl]-1,3,2-dioxaborolane (3c):** yield 90%; mp 80−81 °C; $[\alpha]^{546}{}_{22} = -22$ (*c* = 1.310, $CHCl_3$); IR (KBr) 2922, 1652, 1602, 1497, 1451, 1358, 1118, 912 cm$^{-1}$; $^1$H NMR ($CDCl_3$) *δ* 0.80−1.75 (m, 22H), 2.85 (t, 1H, *J* = 12.8 Hz), 3.01 (dd, 1H, *J* = 5 Hz, 12.8 Hz), 3.24 (dd, 1H, *J* = 5 Hz, 12.8 Hz), 3.87 (m, 2H), 7.0−7.25 (m, 5H); $^{19}$F NMR ($CDCl_3$) *δ* −163.70 (m, 2F), −158.52 (t, 1F, *J* = 20 Hz), −142.15 (m, 2F); $^{13}$C NMR ($CDCl_3$) *δ* 25.77, 25.93, 26.39, 27.40, 28.32, 33.49, 35.61, 42.92, 84.26, 116.24, 126.19, 128.30, 129.15, 134.90, 140.00, 140.42, 142.90; MS (EI) *m*/*z* (species, rel int) 506 ($M^+$, 60), 423 ($M^+ - C_6H_{11}$, 20), 326 ($M^+ - C_6F_5CH$, 20), 270 ($PhCH_2C(C_6F_5^+$, 44), 191 [$(C_6H_{11})_2CHC^+$, 63)], 91 ($PhCH_2^+$, 100), 83 ($C_6H_{11}^+$,92); HRMS calcd for $C_{28}H_{32}F_5O_2B$ ($M^+$) 506.2415, found 506.2421. **X-ray Crystallography.** A suitable crystal was attached to a glass fiber and placed in a low-temperature nitrogen stream.[14] Data for **3c** were collected at 183 K using a Siemens SMART 1000 instrument (Mo Kα radiation, *λ* = 0.710 73 Å) equipped with a Siemens LT-2A low-temperature device. The SHELXTL ver. 5.10 program package was used for structure solution and refinement.[15] The structures were solved by direct methods and refined by full matrix least squares procedures. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included in the refinement at calculated positions using a riding model included in the SHELXTL program.[15] **Data:** monoclinic, *P*2(1), *a* = 10.0354(9) Å, *b* = 9.1807(8) Å, *c* = 13.9660(13) Å, *β* = 91.863-(2)°; *Z* = 2; *F*(000) = 532; 1.308 Mg/m$^3$; *θ*-range 1.46−24.99°; Data/restraints/parameters: 3859/1/325; GOOF 0.963; $R_1$ = 0.0505, $wR_2$ = 0.0897.

**[2(1′*R*),4*R*,5*R*]-4,5-Dicyclohexyl-2-[1-(4-fluorophenyl)-2-phenylethyl]-1,3,2- dioxaborolane (3d):** yield 92%; mp 70 °C; $[\alpha]^{546}{}_{22} = -19$ (*c* = 1.022, $CHCl_3$); IR (KBr) 2926, 1600, 1496, 1448, 1404, 1373, 1241, 1032, 982 cm$^{-1}$; $^1$H NMR ($CDCl_3$) *δ* 0.75−1.74 (m, 22), 2.75 (t, 1H, *J* = 8.6 Hz), 2.95 (dd, 1H, *J* = 7 Hz), 3.15 (dd, 1H, *J* = 7 Hz), 3.78 (m, 2), 6.80−7.30 (m, 9H); $^{19}$F NMR ($CDCl_3$) *δ* −118.57 (m, 1F); $^{13}$C NMR ($CDCl_3$) *δ* 25.81, 25.94, 26.34, 27.19, 28.13, 32.92, 38.65, 42.89, 83.53, 114.66, 115,07, 125.77, 128.03, 128.77, 129.69, 129.85, 137.10, 141.40, 158.61, 163.44; MS (EI) *m*/*z* (species, rel int) 433 ($M^+ - H$, 3), 343 ($M^+ - PhCH_2$, 5), 338 ($M - FC_6H_5$, 100), 191 [$(C_6H_{11})_2CHC^+$, 28)], 91 ($PhCH_2^+$, 22), 83 ($C_6H_{11}^+$,11); HRMS calcd for $C_{28}H_{36}FO_2B$ ($M^+$) 434.2792, found 434.2788.

**[2(1′*R*),4*R*,5*R*]-4,5-Dicyclohexyl-2-[1-[4-(trifluoromethyl)-phenyl]-2-phenylethyl]-1,3,2-dioxaborolane (3e):** yield 90%; viscous liquid; IR $[\alpha]^{546}{}_{22} = -20$ (c = 1.125, $CHCl_3$); (KBr) 2926, 1650, 1602, 1495, *1455*, 1356, 1115, 910, cm$^{-1}$; $^1$H NMR ($CDCl_3$) *δ* 0.80−1.75 (m, 22), 2.85 (t, 1H, *J* = 10.5 Hz), 2.95 (dd, 1H, *J* = 5 Hz), 3.20 (dd, 1H, *J* = 5 Hz), 3.78 (m, 2), 7.0−7.25 (m, 5H), 7.31 (d, 2H, *J* = 8 Hz), 7.48 (d, 2H, *J* = Hz); $^{19}$F NMR ($CDCl_3$) *δ* −62.40 (s, 3F); $^{13}$C NMR ($CDCl_3$) *δ* 25.77, 25.90, 26.31, 27.15, 28.13, 33.49, 42.87, 83.66, 125.15, 125.92, 128.13, 128.74, 143.00, 130.50; MS (EI) *m*/*z* (species, rel int) 484 ($M^+$, 37), 248 ($PhCH_2C(C_6H_4CF_3)^+$, 44), 191 [$(C_6H_{11})_2CHC^+$, 16)], 91 ($PhCH_2^+$, 100), 83 ($C_6H_{11}^+$, 25); HRMS calcd for $C_{29}H_{36}F_3O_2B$ ($M^+$) 484.2760, found 484.2754.

**[2(1′*R*),4*R*,5*R*]-4,5-Dicyclohexyl-2-[1-[3,5-bis(trifluoromethyl)phenyl]-2-phenylethyl]-1,3,2-dioxaborolane (3f):** yield 91%; viscous liquid; $[\alpha]^{546}{}_{22} = -24.2$ (*c* = 1.340, $CHCl_3$); IR (KBr) 2924, 1650, 1604, *1495*, 1450, 1357, 1116, 887 cm$^{-1}$; $^1$H NMR ($CDCl_3$) *δ* 0.80−1.76 (m, 22), 2.80 (t, 1H, *J* = 9 Hz), 2.99 (dd, 1H, *J* = 5.6 Hz), 3.22 (dd, 1H, *J* = 5.6 Hz), 3.85 (m, 2), 7.0−7−8.55 (m, 8H); $^{19}$F NMR ($CDCl_3$) *δ* −63.02 (s, 3F), −63.05 (s, 3F); MS (EI) *m*/*z* (species, rel int) 552 ($M^+$, 12), 469 ($M^+ - C_6H_{11}$, 7), 339 [$M^+ - C_6H_3(CF_3)_2$, 2], 316 ($PhCH_2C(CF_3)_2C_6H_3^+$, 8), 191 [$(C_6H_{11})_2CHC^+$, 10)], 91 ($PhCH_2^+$, 100), 83 ($C_6H_{11}^+$, 13), 69 ($CF_3^+$, 2); HRMS calcd for $C_{30}H_{35}F_6O_2B$ ($M^+$) 552.2634, found 552.2640.

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**[2(1′*R*),4*R*,5*R*]-4,5-Dicyclohexyl-2-[1-(pentafluorophenyl-)ethyl]-1,3,2-dioxaborolane (3g):** Yield, 89%; viscous liquid; $[\alpha]^{546}{}_{22} = -15.5$ ($c = 1.152$, $CHCl_3$); IR (KBr) 2927, 1653, 1498, 1451, 1355, 1394, 1234, 1195, 967 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.80−1.75 (multiplet with a doublet at 1.30, 25H, $J = 7.5$ Hz), 2.76 (q, 1H, $J = 7.6$ Hz), 3.85 (m, 2H); $^{19}F$ NMR ($CDCl_3$) $\delta$ −163.76 (m, 2F), 158.51 (t, 1F, $J = 20$ Hz), −143.42 (m, 2F); $^{13}C$ NMR ($CDCl_3$) $\delta$ 17.0, 25.80, 25.94, 26.44, 27.52, 28.42, 33.51, 42.96, 84.27, 118.70, 134.96, 139.95, 147.39; MS (EI) *m/z* (species, rel int) 430 ($M^+$, 41), 347 ($M^+ - C_6H_{11}$, 100), 191 [$(C_6H_{11})_2CHC^+$, 15)], 83 ($C_6H_{11}^+$, 92); HRMS calcd for $C_{22}H_{28}F_5O_2B$ ($M^+$) 430.2102, found 430.2117.

**[2(1′*R*),4*R*,5*R*]-4,5-Dicyclohexyl-2-[1-(4-fluorophenyl)-ethyl]-1,3,2-dioxaborolane (3h):** yield 92%; viscous liquid; $[\alpha]^{546}{}_2{}^2 = -16.4$ ($c = 1220$, $CHCl_3$); IR (KBr) 2926, 1601, 1506, 1450, 1353, 1223, 1157, 1094, 985 $cm^{-1}$: $^1H$ NMR ($CDCl_3$) $\delta$ 0.80−1.74 (multiplet with a doublet at 1.31, 25H, $J = 7.5$ Hz), 2.45 (q, 1H, $J = 7.5$ Hz), 3.84 (m, 2H); $^{19}F$ NMR ($CDCl_3$) $\delta$ −119.21 (t, 1F, $J = 12.5$ Hz), $^{13}C$ NMR ($CDCl_3$) $\delta$ 17.19, 24.00, 25.87, 25.97, 26.45, 27.25, 28.20, 83.44, 114.75, 128.87, 140.61, 158.45, 163.27; MS (EI) *m/z* (species, rel int) 458 ($M^+$, 46), 375 ($M^+ - CH_3$, 18), 123 [$CH_3CH(C_6H_4F)$, 18], 107 ($M^+ - C_6H_4FC$, 41) 83 ($C_6H_{11}^+$, 51); HRMS calcd for $C_{22}H_{32}FO_2B$ ($M^+$) 358.2479, found 358.2479.

**[2(1′*R*),4*R*,5*R*]-4,5-Dicyclohexyl-2-[1-[4-(trifluoromethyl)-phenyl]ethyl]-1,3,2-dioxaborolane (3i):** yield 91%; viscous liquid; $[\alpha]^{546}{}_{22} = -13$ ($c = 1.415$, $CHCl_3$); IR (KBr) 2926, 1695, 1618, 1452, 1408, 1323, 1236, 1166, 891 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.80−1.74 (multiplet with a doublet at 1.29, 25H, $J = 7.5$ Hz), 2.74 (q, 1H, $J = 7.5$ Hz), 3.82 (m, 2H), 7.44 (d, 2H, $J = 8$ Hz), 7.55 (d, 2H, $J = 8$ Hz); $^{19}F$ NMR ($CDCl_3$) $\delta$ −62.10 (s, 3F); MS (EI) *m/z* (species, rel int) 408 ($M^+$, 41), 325 ($M^+ - C_6H_{11}$, 100), 191 [$(C_6H_{11})_2CHC^+$, 12)], 83 ($C_6H_{11}^+$, 78).

**[2(1′*R*),4*R*,5*R*]-4,5-Dicyclohexyl-2-[1-[3,5-bis(trifluoro-methyl)phenyl]ethyl]-1,3,2-dioxaborolane (3j):** yield 89%; viscous liquid; $[\alpha]^{546}{}_{22} = -12$ ($c = 1.140$, $CHCl_3$); IR (KBr) 2922, 1652, 1600, 1490, 1450, 1358, 1110, 889 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.80−1.76 (multiplet with a doublet at 1.28, 25H, $J = 7.5$ Hz), 2.72 (q, 1H, $J = 7.5$ Hz), 3.84 (m, 2H), 7.50 (m, 2H), 7.75 (m, 1H); $^{19}F$ NMR ($CDCl_3$) $\delta$ −63.04 (s, 3F), −63.07 (s, 3F); MS (EI) *m/z* (species, rel int) 476 ($M^+$, 22), 393 ($M^+ - C_6H_{11}$, 100), 191 [$(C_6H_{11})_2CHC^+$, 17)], 83 ($C_6H_{11}^+$, 12), 69 ($CF_3^+$, 5); HRMS calcd for $C_{24}H_{31}F_6O_2$ B ($M^+$) 476.2321, found 476.2318.

**General Procedure for the Synthesis of α-Fluorinated Aryl Alcohols.** Aqueous 3 M sodium hydroxide (25 mL) and a solution of boronic esters **(3c−j,** 8 mmol) in diethyl ether (150 mL) were stirred and cooled with an ice bath during the portionwise addition of 30% hydrogen peroxide (25 mL) over a period of 1 h. The reaction mixture was stirred for 15 h. More ether (100 mL) was added. The ether phase was washed with water, dried over magnesium sulfate and filtered. Removal of ether at low pressure yielded a mixture of alcohols **(4c−j)** and [(*R*)-(*R**,*R**)]-1,2-dicyclohexyl-1,2-ethanediol. The latter was recovered in ∼90% yield by addition of pentane (15 mL) and crystallization at 0 °C. Fluorinated aryl alcohols were isolated in >79% yield by using column chromatography eluting with ether/pentane (1:3) mixture.

**(*R*)-1-(Pentafluorophenyl)-2-phenylethanol (4c):** yield 89%; mp 58−59 °C; $[\alpha]^{546}{}_{22} = +20$ ($c = 2.3$, $CHCl_3$); ee > 99%; (KBr) 3169, 2920, 1651, 1499, 1451, 1357, 1123, 1064, 999, 954 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.18 (s, 1H), 3.07 (dd, 1H, $J = 6.5$ Hz), 3.29 (dd, 1H, $J = 8$ Hz), 5.25 (t, 1H, $J = 6.5$ Hz), 7.0−7.35 (m, 5H); $^{19}F$ NMR ($CDCl^3$) $\delta$ −162.01 (m, 2F), −154.97 (t, 1F, $J =$ 20 Hz), −143.59 (m, 2); $^{13}C$ NMR ($CDCl_3$) $\delta$ 43.14, 67.37, 116.24, 127.18, 128.75, 129.11, 134.92, 141.00, 142.50, 147.32; MS (EI) *m/z* (species, rel int) 288 ($M^+$, 1), 197 ($M^+ - PhCH_2$, 40), 92 ($PhCH_2$ + H, 100), 91 ($PhCH_2^+$, 88). Anal. Calcd for $C_{14}H_9F_{50}$: C, 58.34; H, 3.15. Found: C, 58.42; H, 3.02.

**(*R*)-1-(4-Fluorophenyl)-2-phenylethanol (4d):** yield 82%; mp 67 °C; $[\alpha]^{546}{}_{22} = +22$ ($c = 1.140$, $CHCl_3$); ee > 99%; IR (KBr) 3400, 2926, 1495, 1445, 1406, 1370, 1240, 1030, 985 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) 1.70 (s, 1H), 2.94 (dd, 1H, $J = 7$ Hz), 3.0 (dd, 1H, $J = 7$ Hz), 4.95 (t, 1H, $J = 8.6$ Hz), 4.86 (t, 1H, $J = 6.0$ Hz), 6.80−7.34 (m, 9H); $^{19}F$ NMR ($CDCl_3$) $\delta$ −115.20 (m, 1F,); MS (EI) *m/z* (species, rel int) 216 ($M^+$, 2), 199 ($M^+$ −OH, 2), 125 ($M^+ - PhCH_2$, 99), 92 ($PhCH_2^+$ + H, 100), 77 ($Ph^+$, 17). Anal. Calcd for $C_{14}H_{13}FO$: C, 77.74; H, 6.06. Found: C, 77.53; H, 6.18.

**(*R*)-1-[(4-Trifluoromethyl)phenyl]-2-phenylethanol (4e):** yield 80%; mp 57−58 °C; $[\alpha]^{546}{}_{22} = +18.5$ ($c = 1.200$, $CHCl_3$); ee > 99%; IR (KBr) 3396, 2926, 1618, 1494, 1448, 1417, 1326, 1165, 1124, 1067 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.13 (s, 1H), 2.90 (dd, 2H, $J = 5$ Hz), 3.02 (dd, 1H, $J = 5.0$ Hz), 4.91 (dd, 1H, $J = 5$ Hz), 7.0−7.4 (m, 5H), 7.42, (d, 2H, $J = 8$ Hz), 7.57 (d, 2H, $J = 8$ Hz); $^{19}F$ NMR ($CDCl_3$) $\delta$ −62.57 (s, 3F); $^{13}C$ NMR ($CDCl_3$) $\delta$ 46.05, 74.61, 124.30 (q, $J_{C-F} = 282$ Hz), 125.24, 125.31, 126.15, 126.86, 128.62, 129.48, 137.28, 147.6; MS (EI) *m/z* (species, rel int) 267 ($M^+$ + H, 1), 248 ($M^+ - H_2O$, 2), 175 ($M^+ - PhCH_2$, 19), 145 ($CF_3C_6H_4^+$, 5), 92 ($PhCH_2$ + H, 100), 91 ($PhCH_2^+$, 50), 77 ($Ph^+$, 4).

**(*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]-2-phenylethanol (4f):** yield 84%; viscous liquid; $[\alpha]^{546}{}_{22} = +17.4$ ($c = 1.113$, $CHCl_3$); ee > 99%; IR (KBr) 3408, 2931, 1707, 1614, 1462, 1384, 1278, 1173, 1134, 1076, 943 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.36 (s, 1H), 2.92 (dd, 2H, $J = 5$ Hz), 3.02 (dd, 1H, $J = 5.0$ Hz), 4.99 (t, 1H, $J = 5$ Hz), 7.1 (m, 1H), 7.26, (m, 2H,), 7.77 (s, 1H); $^{19}F$ NMR ($CDCl_3$) $\delta$ −63.08 (s, 6F); $^{13}C$ NMR ($CDCl_3$) $\delta$ 46.10, 74.13, 115.83, 120.62, 124.0 (q, $J_{C-F} = 283.5$), 121.44, 126.07, 127.22, 128.83, 129.28, 129.47, 130.62, 131.29, 131.94, 132.61, 133.22; MS (EI) *m/z* (species, rel int) 334 ($M^+$, 1), 316 ($M^+ - H_2O$, 1), 315 ($M^+$ − F, 1), 243 ($M^+$-$C_6H_5CH_2$, 10), 195 [$M^+ - (CF_3 + CF_3$ + H), 13], 92 ($PhCH_2$ + H, 100), 91 ($PhCH_2^+$, 67), 69 ($CF_3^+$, 2). Anal. Calcd for $C_{16}H_{12}F_6O$: C, 57.47; H, 3.62. Found: C, 57.57; H, 3.98.

**(*R*)-1-(Pentafluorophenyl)ethanol[16] (4g):** yield 86%; mp 41 °C; $[\alpha]^{546}{}_{22} = +13$ ($c = 1.130$, $CHCl_3$); ee > 99%; IR (KBr) 3365, 1653, 1505,1304, 1134, 1084, 1043, 973, 936, 865 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.62 (d, 3H, $J = 6.7$ Hz), 2.18 (broad, s, 1H), 5.22 (q, 1H, $J = 6.7$ Hz); $^{19}F$ NMR ($CDCl_3$) $\delta$ −162.15 (m, 2F), 155.76 (t, 1F, $J = 20.5$ Hz), − 144.80 (m, 2); $^{13}C$ NMR ($CDCl_3$) $\delta$ 23.16, 62.28, 118.10, 136.12, 139.35, 143.25, 146.50; MS (EI) *m/z* (species, rel int) 212 ($M^+$, 10), 197 ($M^+ - CH_3$, 100), 195 ($M^+ - OH$, 8), 167 ($C_6F_5^+$, 4), 45 ($CH_3CHOH^+$, 10). Anal. Calcd for $C_8H_5F_5O$: C, 45.28; H, 2.38. Found: C, 45.28; H, 2.38.

**(*R*)-1-(4-Fluorophenyl)ethanol[17] (4h):** yield 85%; viscous liquid; $[\alpha]^{546}{}_{22} = +27$ ($c = 1.270$, $CHCl_3$); ee > 99%; IR (film) 3367, 2962, 1657, 1500,1306, 1138, 1081, 1040, 978, 934 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.50 (d, 3H, $J = 6.5$ Hz), 2.0 (broad, s, 1H), 4.95 (q, 1H, $J = 6.5$ Hz), 6.6 (d, 2H, $J = 6$ Hz), 7.50 (d, 2H, $J =$ 6 Hz); $^{19}F$ NMR ($CDCl_3$) $\delta$ −118.20 (m, 1F); MS (El) *m/z* (species, rel int) 140 ($M^+$, 8), 125 ($M^+ - CH_3$, 100), 123 ($M^+ - OH$, 7).

**(*R*)-1-[4-(Trifluoromethyl)phenyl]ethanol[17] (4i):** yield 80%; viscous liquid; $[\alpha]^{546}{}_{22} = +28$ ($c = 1.115$, $CHCl_3$); ee > 99%; IR (KBr) 3360, 1650, 1496,1300, 1130, 1088, 1045, 970 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.50 (d, 3H, $J = 6.6$ Hz), 2.20 (broad, s, 1H), 5.0 (q, 1H, $J = 6.6$ Hz), 7.50 (d, 2H, $J = 8.8$ Hz), 7.65 (d, 2H, $J$ = 8.8 Hz); $^{19}F$ NMR ($CDCl_3$) $\delta$ −63.0 (s, 3F); MS (EI) *m/z* (species, rel int) 190 ($M^+$, 8), 175 ($M^+ - CH_3$, 100), 173 ($M^+ - OH$, 7), 69 ($CF_3^+$, 8).

**(*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethanol (4j):** yield 82%; viscous liquid; $[\alpha]^{546}{}_{22} = +16$ ($c = 1.204$, $CHCl_3$); ee > 99%; IR (film) 3368, 1658, 1500, 1298, 1138, 1080, 968, $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.50 (d, 3H, $J = 6.6$ Hz), 2.40 (broad, s, 1H), 4.90 (q, 1H, $J = 6.6$ Hz) 7.20, (m, 2H,), 7.75 (s, 1H); $^{19}F$ NMR ($CDCl_3$) $\delta$ −63.01 (s, 3F), − 63.05 (s, 3F); MS (EI) *m/z* (species, rel int) 258 ($M^+$, 10), 243 ($M^+ - CH_3$, 100), 226 ($M^+ - OH$, 8), 69($CF_3^+$, 14).

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**Supporting Information Available:** Crystal data and structure refinement, atomic coordinates, bond lengths and bond angles, anisotropic displacement parameters, hydrogen coordinates, and crystal packing diagram for **3c**. This material is available free of charge via the Internet at http://pubs.org.

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