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Asymmetric Fluorination of α-Branched Aldehydes by Chiral Primary Amine Catalysis: Reagent-controlled Enantioselectivity Switch

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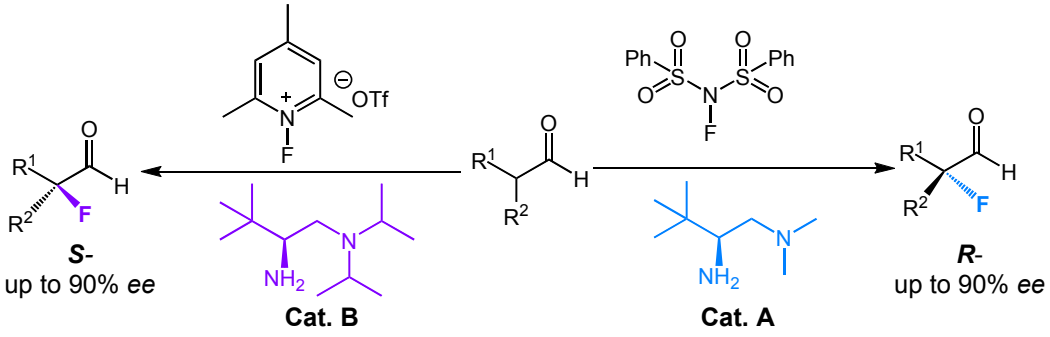


Keywords: asymmetric fluorination, enantioselectivity switch, enamine catalysis, α-branched aldehydes.

Abstract: Asymmetric fluorination of α-branched aldehydes catalyzed by chiral primary amines under mild conditions has been developed. Both enantiomers could be obtained with good yields (up to 96%) and high enantioselectivity (up to 90% *ee*) by a simple swap of the fluorination reagents.

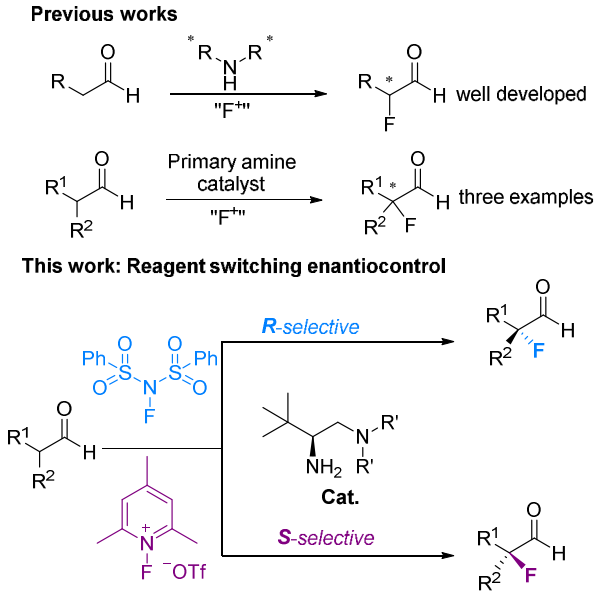
Stereoselective install of fluorine atom is of significant synthetic interests due to the prevalence of C-F bond in bioactive compounds.[1,2] On this basis, tremendous efforts have been devoted to the development of new methods for catalytic enantioselective construction of C-F bond. In this regard, aminocatalysis has

become an enabling strategy for enantioselective α-C-F bond formation of carbonyls. In 2005, Jørgensen, Barbas and MacMillan independently reported α-fluorination of linear aldehydes catalyzed by chiral secondary amine catalysts.[3] The same reaction has also received a plethora of further developments.[4] However, α-branched aldehydes remain difficult substrates despite of these advances. The lower tendency to form enamine as well as the variable enamine geometry are two major issues impeding the enamine reactions with α-branched carbonyls including both ketones and aldehydes.[5]

Chiral primary amines have been proved to be viable catalysts for the reactions with α-branched ketones/aldehydes. Recently, chiral primary amines have also been reported in the enantioselective fluorination of α-branched aldehydes. In 2006, Jørgensen reported a chiral amine catalyst for the reaction of α-branched aldehydes with good enantioselectivitiy, but low yields.[6] In 2015, Jacobsen developed a chiral primary amine-amide catalyst for the same reaction with improved activity.[7] Very recently, Shibatomi and co-workers designed and synthesized a chiral binapthyl-derived primary amine for enantioselective fluorination of α-branched aldehydes with generally good activity and enantioselectivity.[8]

In principle, the stereospecific synthesis of both enantiomers of an organic compound requires the employment of both enantiomers of a chiral catalyst, respectively.[11] The use of a single chiral catalyst to abtain both enantiomers of products is an attractive yet challenging aim in asymmetric catalysis, and enantioselective switch with a single chiral resource has been actively pursued for this end.[12] Recently, we reported a chiral primary amine catalyzed asymmetric fluorination of β-ketocarbonyls and simple swap of the fluoro-reagents led to opposite chiral induction with the same chiral primary amine catalyst.[9,10] This reagent-switching enantioselective fluorination was further explored in the α-fluorination of α-branched aldehydes. Herein, we reported a reagent-switching enantioselective fluorination of α-branched aldehydes (Scheme 1).

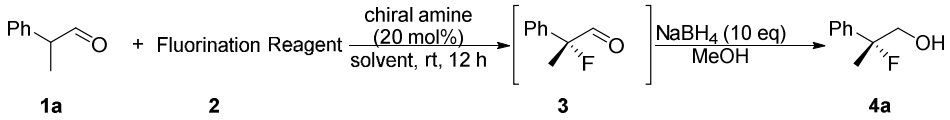
SCHEME 1. Asymmetric fluorination of aldehydes under enamine catalysis.



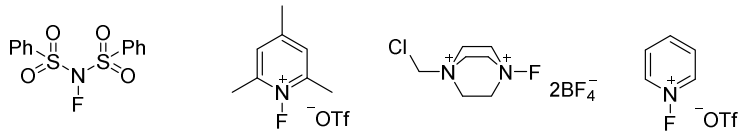
Initially, we treated 2-phenylpropionaldehyde **1a** with fluorination reagent **2** in the presence of 20 mol% of catalyst **I**/DNBA in $CHCl_3$ for 12 h. Although the process proved to be feasible, no switch of chiral induction was noted among different fluorination reagents (Table 1, entries 1-3). When we performed the reaction in MeOH, the switch of enantioselectivity was clearly observed (Table 1, entries 5 and 6 *vs* entries 2 and 3). The use of cationic fluoro-reagents **2b** and **2c** led to opposite chiral induction compared to that with a neutral reagent **2a**. The reagent **2a** and **2b** were selected for the subsequent optimization. We then found that using trifluoromethanesulfonic acid as co-catalyst led to slightly better results (entries 7 and 8). Further optimization of the reaction conditions was carried out by examing different solvents. It was found that *R*-selective process with **2a** worked favorably in low-polar solvents such as $CHCl_3$, whereas strong-polar or protonic solvents favored the *S*-selective process with **2b**. The switch of solvent from $CHCl_3$ to methanol could even reverse the chiral induction with same fluorinated reagents (entries 2 and 3, vs entries 5 and 6, respectively), indicating two co-existing and competing stereo-controlling interactions for this reaction. DMF was identified as the optimal solvent for the *S*-selective process (entry 11). Different chiral primary amine catalysts were then screened in order to improve the enantioselectivity.

Gratifyingly, upon changing the propyl secondary amine moiety to dimethyl tertiary amine, good values of enantioselectivity were reached for *R*-selective process (entry 9). A bulky diisopropyl tertiary amino group was found to favor the *S*-selective process (entry 12). The use of

Table 1. Optimization of the reaction conditions[a]



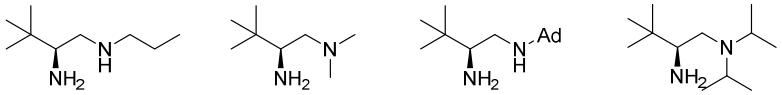
1a **2** **3** **4a**



2a **2b** **2c** **2d**

Entry	Amine catalyst	Fluorination reagent	Solvent	Yield (%)[b]	*ee* (%)[c]
1	**I**/DNBA	**2a**	$CHCl_3$	66	74 (*R*-)
2	**I**/DNBA	**2b**	$CHCl_3$	43	23
3	**I**/DNBA	**2c**	$CHCl_3$	76	42
4	**I**/DNBA	**2a**	MeOH	52	22
5	**I**/DNBA	**2b**	MeOH	56	-64 (*S*-)
6	**I**/DNBA	**2c**	MeOH	72	-39
7	**I**/HOTf	**2a**	$CHCl_3$	66	79
8	**I**/HOTf	**2b**	MeOH	62	-70
9	**II**/HOTf	**2a**	$CHCl_3$	81	86
10	**II**/HOTf	**2b**	MeOH	42	-53
11	**I**/HOTf	**2b**	DMF	42	-72
12	**IV**/HOTf	**2b**	DMF	46	-86
13	**IV**/HOTf	**2d**	DMF	34	-73
14[d]	**II/HOTf**	**2a**	**$CHCl_3$**	**92(86)**	**85**
15[d]	**IV/HOTf**	**2b**	**DMF**	**84(82)**	**-85**

[a]All reactions were carried out with 1.5 equivalent of fluorination reagent **2** and 20 mol% of amine catalyst respect to 2-phenylpropionaldehyde **1a** (0.10 mmol) in 0.5 ml solvent unless otherwise noted. DNBA: 2,4-dinitrobenzoic acid. [b]Yields were determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as an internal standard. The yields in the parentheses are isolated. [c]Determined by HPLC on a chiral stationary phase. [d]Reaction conditions: **1a** (0.36 mmol), **2** (0.30 mmol), amine catalyst (20 mol%) in solvent (1.5 mL) at room temperature for 12 h.

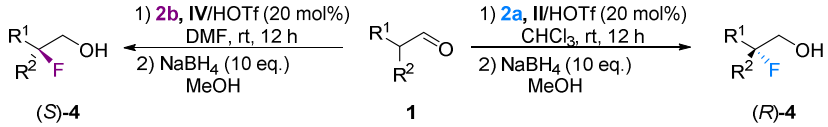


I II III IV

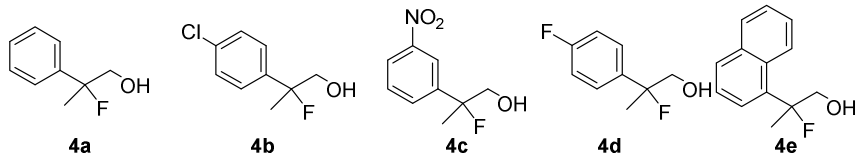
unsubstituted pyridinium **2d** showed slightly lower enantioselectivity (entry 13), indicating steric effect in this case. The reaction could be conducted at 0.3 mmol scale with similar outcome (entries 14 and 15). Thus, we have optimized the parameters required for optimal results. For the *R*-selective process, the best reaction condition is treating **2a** with 1.2 equivalent of **1a** in the presence of amine catalyst **II**/ HOTf (1:1) in $CHCl_3$ at room temperature for 12 h, providing the product with 86% yield and 85% *ee*. For the *S*-selective process, the best reaction condition is treating **2b** with 1.2 equiv. of **1a** in the presence of amine catalyst **IV**/ HOTf in DMF at room temperature for 12 h, providing the product with 82% yield and -85% *ee*.

With the optimal results in hand, we firstly investigated the substrates scope for the *R*-selective process.

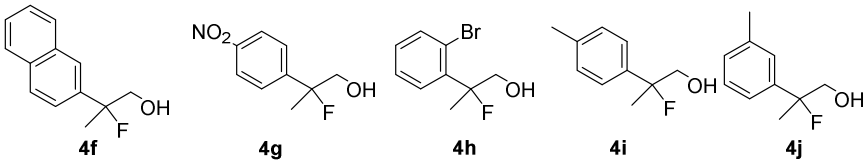
Table 2. Scope of products[a]



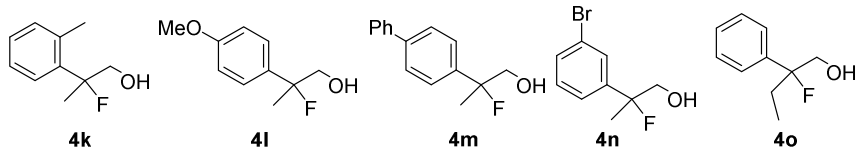
(*S*)-**4** **1** (*R*)-**4**



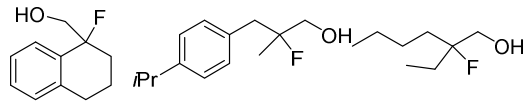
	4a	**4b**	**4c**	**4d**	**4e**
(*R*)-:	87%, 85% *ee*	93%, 85% (99%)[b] *ee*	90%, 84% *ee*	87%, 78% *ee*	82%, 86% *ee*
(*S*)-:	80%, 85% *ee*	82%, 86% (97%)[b] *ee*	92%, 87% *ee*	84%, 84% *ee*	84%, 69% *ee*



	4f	**4g**	**4h**	**4i**	**4j**
(*R*)-:	96%, 85% *ee*	84%, 83% *ee*	80%, 74% *ee*	90%, 85% *ee*	82%, 84% *ee*
(*S*)-:	94%, 88% *ee*	82%, 87% *ee*	75%, 78% *ee*	81%, 84% *ee*	88%, 87% *ee*



	4k	**4l**	**4m**	**4n**	**4o**
(*R*)-:	28%, 86% *ee*	n.d. (see txt)	83%, 90% *ee*	84%, 85% *ee*	81%, 60% *ee*
(*S*)-:	40%, 75% *ee*		72%, 87% *ee*	76%, 85% *ee*	82%, 69% *ee*



	4p	**4q**	**4r**
(*R*)-:	52%, 86% *ee*	62%, 52% *ee*	25%, 7% *ee*
(*S*)-:	55%, 90% *ee*	57%, 27% *ee*	12%, *rac*

[a]General conditions: **1a** (0.36 mmol), **2** (0.3 mmol), amine catalyst (20 mol%) in solvent at room temperature for 12 h. Absolute configurations assigned based on comparison of optical rotations to published data. Isolated yield of **4** are described. *Ee* was determined by GC or HPLC on a chiral stationary phase. [b]*Ee* after recrystallization.

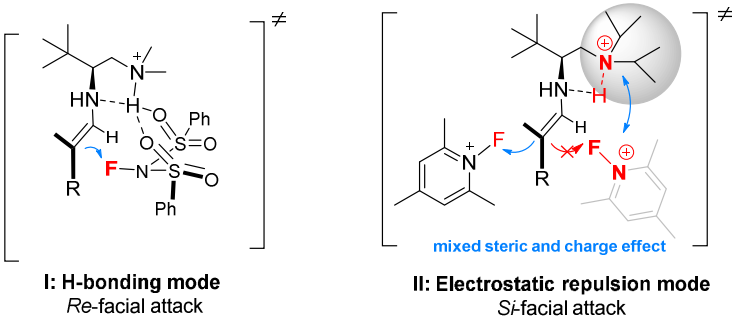
As shown in Table 2, a variety of α-alkyl-α-aryl aldehydes bearing either electron-withdrawing or electron-donating groups on the aryl ring were examined in present fluorination reaction with good yields and high enantioselectivity (Table 2, **4a**-**4g**). *Ortho*-substituted aryl aldehydes such as **1h** and **1k** afforded the products (**4h** and **4k**) with inferior activity or enantioselectivity. Electron-rich aryl aldehyde **1l** showed good reactivity, however, the desired product could not be isolated likely due to its instability. An α-ethyl aldehyde **1o** could also be applied with 81% yield and 60% *ee*. 2-(Pyridin-2-yl)propanal has also been examined, showing unfortunately no reaction in both cases, and it is likely the basicity of pyridine moiety is

detrimental to the electrophilic reaction. The reaction also worked well with a cyclic aldehyde **1p** with 52% yield and 86% *ee*. α, α-Dialkyl aldehydes such as **1q** and **1r** have also been examined in the reactions, showing unfortunately poor activity and enantioselectivity (**4q** and **4r**).

In the *S*-selective reactions, we also tested the same substrates scope. The switch of enantioselectivity took place in all cases. In most instances, the results were comparable to those obtained in the *R*-selective reactions. As shown with **4b**, enantiomeric excess for both enantiomers could be enriched by a single recrystallization from hexane.

On the basis of previous studies,[7,9,10] we proposed a H-bonding mode (**I**) and an electrostatic repulsion mode (**II**) to account for the *R*- and *S*- selectivity, respectively (Scheme 2). Chiral primary amine catalyst would react with α-branched aldehyde to form predominantly *E*-enamine intermediate. H-bonding between the protonated tertiary amine and sulfonyl group of NFSI would facilitate *Re*-facial fluorination. On the other hand, a mixed steric and charge repulsion effect would disfavor the *Re*-facial attack and push the cationic N-fluoropyridinium moiety for *Si*-facial fluorination. The observed polar solvent effect is clearly

SCHEME 2. Proposed transition states.



I: H-bonding mode
Re-facial attack

II: Electrostatic repulsion mode
Si-facial attack

in line with this electrostatic repulsion effect, as polar reaction media would favor charge associated interactions (Table 1, entries 1-6). In addition, the observation that less hindered NFPy **2d** led to lower *ee* (73% *ee*, Table 1, entry 13) provides further evidence to the charge repulsion mode.

In conclusion, we have developed an organocatalytic asymmetric fluorination of α-branched aldehydes **1.** By using two different fluorination reagents**,** opposite chiral induction could be achieved by the same configured chiral primary amine catalyst with good yields and high enantioselectivity.

Experimental section

General Methods. All commercial reagents were used without further purification unless otherwise noted. The corresponding aldehydes were prepared according to reported procedures. NMR spectra were recorded on *Bruker AV 400* and *Bruker Avance 500* spectrometers. ^{1}H NMR spectra were obtained at 400 or 500 MHz in $CDCl_3$ unless otherwise noted. ^{13}C NMR spectra were obtained at 101 or 126 MHz using a proton-decoupled pulse sequence and are tabulated by observed peak. Chemical shifts were reported in parts per million (ppm) and referenced to 7.27 and 77.00 ppm respectively. Coupling constants were expressed in Hertz (Hz). The following abbreviations were used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, br = broad. ^{19}F spectra were obtained at 377 MHz using a proton-decoupled pulse sequence in the presence of fluorobenzene as an internal standard. High resolution mass spectra were obtained using electrospray ionization (APCI and EI). The enantiomeric excesses were determined by HPLC analysis on Chiral Daicel Chiralpak OD-H, OJ-H, AS-H, AD-H or GC analysis on chiral stationary phases (CYCLOSIL-B: 30mm · 0.250mm). Optical rotation were measured on a commercial polarimeter and reported as follows: $[\alpha]_D^{25}$ (c = g/100 mL, solvent).

General Procedure (A) for the Synthesis of (*R*)-α-Branched Aldehydes: To a flame-dried tube equipped with a magnetic stir bar were added α-branched aldehyde (**1**, 0.36 mmol), amine catalyst (**II**/HOTf, 18mg, 0.06 mmol) and NFSI (**2a**, 94.5 mg, 0.30 mmol). The resulting mixture was then diluted with 1.5 mL of $CHCl_3$. The reaction was conducted at room temperature for 12 h, then poured into MeOH (2 mL) at 0 °C. To this solution, $NaBH_4$ (114 mg, 3.0 mmol, 10 equiv.) was added, and the mixture was stirred at room temperature for 1 h. The reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with CH_2Cl_2 (5 mL x 3). The organic layers were combined and dried over Na_2SO_4, concentrated, and chromatographed on silica gel with hexane:Et_2O solution (5:1 to 1:1) to give (*R*)-**4**.

General Procedure (B) for the Synthesis of (*S*)-α-Branched Aldehydes: To a flame-dried tube equipped with a magnetic stir bar were added α-branched aldehyde (1, 0.36 mmol), amine catalyst (IV/HOTf, 21mg, 0.06 mmol) and NFCO-OTf (2b, 86.7 mg, 0.30 mmol). The resulting mixture was diluted with 1.5 mL of DMF. The reaction was conducted at room temperature for 12 h, then poured into MeOH (2 mL) at 0 °C. To this solution, $NaBH_4$ (114 mg, 3.0 mmol, 10 equiv) was added, and the mixture was stirred at room temperature for 1 h. The reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted with CH_2Cl_2 (5 mL x 3). The organic layers were combined and dried over Na_2SO_4, concentrated, and chromatographed on silica gel with hexane:Et_2O solution (5:1 to 1:1) to give (*S*)-4.

2-fluoro-2-phenylpropan-1-ol (4a): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4a** (40.2 mg, 87%) and (*S*)-**4a** (36.9 mg, 80%) as colorless oil: IR (thin film, cm^{-1}) 3380 (br), 2961, 2928, 1496, 1448, 1379, 1028, 762; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43 - 7.29 (m, 5 H), 3.97 - 3.59 (m, 2 H), 1.85 - 1.77 (m, 1 H), 1.70 (d, J = 22.6 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.6 (d, J = 21.4 Hz), 128.6 (d, J = 1.3 Hz), 128.0, 124.6 (d, J = 9.3 Hz), 98.0 (d, J = 172.2 Hz), 69.7 (d, J = 25.1 Hz), 23.3 (d, J = 24.6 Hz); ^{19}F NMR

(377 MHz, $CDCl_3$) δ -157.2 (s); HPLC analysis: Daicel Chiralpak AS-H, flow rate =1.0 ml/min, λ=210 nm, hexane/iso-propanol = 98:2, (*R*)-**4a**: 85% *ee*; $[\alpha]_D^{25}$ = -10.5 (c = 1.10, $CHCl_3$), retention time: 12.8 min (minor) and 14.6 min (major); (*S*)-**4a**: 85% *ee*; $[\alpha]_D^{25}$ = 9.8 (c = 1.05, $CHCl_3$), retention time: 12.6 min (major) and 14.4 min (minor); The spectroscopic data for **4a** matched those described in the literature; For the *R*-enantiomer 80% *ee*; $[\alpha]_D^{23}$ = -9.4 (c = 1.1, $CHCl_3$) is reported in the literature.[7] For the *S*-enantiomer 95% *ee*; $[\alpha]_D^{22}$ = 14.3 (c = 0.87, $CHCl_3$) is reported in the literature.[8]

2-(4-chlorophenyl)-2-fluoropropan-1-ol (4b): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4b** (52.6 mg, 93%) and (*S*)-**4b** (46.4 mg, 82%) as white solid: IR (thin film, cm^{-1}) 3361(br),2995, 2924, 1599, 1493, 1403, 1369, 1255, 1129, 1090, 751; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.5 Hz, 2 H), 7.31 (t, *J* = 5.8 Hz, 2 H), 3.88 – 3.66 (m, 2 H), 1.81 (s, 1 H), 1.68 (d, *J* = 22.6 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.2 (d, *J* = 22.1 Hz), 134.0, 128.8 (d, *J* = 1.1 Hz), 126.1 (d, *J* = 9.3 Hz), 97.7 (d, *J* = 172.9 Hz), 69.5 (d, *J* = 25.2 Hz), 23.3 (d, *J* = 24.6 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -156.82 (s); HPLC analysis: Daicel Chiralpak AD-H, flow rate =1.0 ml/min, λ=210 nm, hexane/iso-propanol = 95:5, (*R*)-**4b**: 85% *ee*; $[\alpha]_D^{25}$ = -11.6 (c = 1.45, $CHCl_3$), retention time: 11.5 min (major) and 15.4 min (minor); (*S*)-**4b**: 86% *ee*; $[\alpha]_D^{25}$ = 12.5 (c = 1.55, $CHCl_3$), retention time: 11.5 min (minor) and 15.4 min (major); (*R*)-**4b**(after recrystallized from pentane): 99 % *ee*; retention time: 11.3 min (major) and 14.6 min (minor); (*S*)-**4b**(after recrystallized from pentane): 97 % *ee*; retention time: 11.3 min (major) and 14.6 min (minor); The spectroscopic data for **4b** matched those described in the literature.[7]

2-fluoro-2-(3-nitrophenyl)propan-1-ol (4c): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 1:1) to give (*R*)-**4c** (53.7 mg, 90%) and (*S*)-**4c** (54.9 mg, 92%) as yellow oil: IR (thin film, cm^{-1}) 3388(br), 2987, 2925, 1582, 1530, 1481, 1456,

1251, 1110, 843; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (t, *J* = 1.8 Hz, 1 H), 8.18 (ddd, *J* = 8.1, 2.0, 0.8 Hz, 1 H), 7.71 (d, *J* = 7.8 Hz, 1 H), 7.57 (t, *J* = 8.0 Hz, 1 H), 3.94 – 3.73 (m, 2 H), 2.08 (s, 1 H), 1.73 (d, *J* = 22.5 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 144.0 (d, *J* = 22.7 Hz), 130.9 (d, *J* = 9.2 Hz), 129.7, 123.0, 120.0 (d, *J* = 10.5 Hz), 97.4 (d, *J* = 174.7 Hz), 69.2 (d, *J* = 25.1 Hz), 23.4 (d, *J* = 24.4 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -156.93; HRMS (APCI-orbitrap) m/z: $[M + H]^+$ Calcd for $C_9H_{11}FNO_3$ 200.0717; Found 200.0710; HPLC analysis: Daicel Chiralpak OJ-H, flow rate =0.5 ml/min, λ=210 nm, hexane/iso-propanol = 95:5, (*R*)-**4c**: 84% *ee*; $[\alpha]_D^{25}$ = -8.2 (c = 1.20, $CHCl_3$), retention time: 60.7 min (major) and 63.7 min (minor); (*S*)-**4c**: 87% *ee*; $[\alpha]_D^{25}$ = 9.2 (c = 1.65, $CHCl_3$), retention time: 61.2 min (minor) and 62.8 min (major).

2-fluoro-2-(4-fluorophenyl)propan-1-ol (4d): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4d** (44.9 mg, 87%) and (*S*)-**4d** (43.3 mg, 84%) as colorless oil: IR (thin film, cm^{-1}) 3366(br), 2932, 1605, 1512, 1456, 1408, 1232, 1192, 1015, 724; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.30 (m, 2 H), 7.07 (t, *J* = 8.5 Hz, 2 H), 3.90 – 3.67 (m, 2 H), 1.84 (t, *J* = 6.6 Hz, 1 H), 1.69 (d, *J* = 22.6 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ162.5 (d, *J* = 248.1 Hz), 137.5 (dd, *J* = 22.2, 3.2 Hz), 129.1 – 123.4 (m), 115.5 (d, *J* = 22.4 Hz), 97.7 (d, *J* = 172.3 Hz), 69.7 (d, *J* = 25.4 Hz), 23.4 (d, *J* = 24.6 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -114.68, -155.76; HPLC analysis: Daicel Chiralpak AD-H, flow rate =1 ml/min, λ=210 nm, hexane/iso-propanol = 95:5, (*R*)-**4d**: 78% *ee*; $[\alpha]_D^{25}$ = -9.1 (c = 1.50, $CHCl_3$), retention time: 11.2 min (major) and 13.0 min (minor); (*S*)-**4d**: 84% *ee*; $[\alpha]_D^{25}$ = 10.2 (c = 1.30, $CHCl_3$), retention time: 11.2 min (minor) and 12.9 min (major); The spectroscopic data for **4c** matched those described in the literature.[8]

2-fluoro-2-(naphthalen-1-yl)propan-1-ol (4e): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4e** (50.2 mg,

82%) and (*S*)-**4e** (51.4 mg, 84%) as colorless oil: IR (thin film, cm^{-1}) 3384(br), 3051, 2932, 1599, 1510, 1455, 1381, 1189, 775; ^1H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.1 Hz, 1 H), 7.91 – 7.79 (m, 2 H), 7.58 (d, *J* = 7.3 Hz, 1 H), 7.54 – 7.41 (m, 3 H), 4.37 – 3.97 (m, 2 H), 1.97 (d, *J* = 23.1 Hz, 3 H), 1.97 (s, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.6 (d, *J* = 19.3 Hz), 134.8, 130.4, 129.7, 129.4, 126.3, 125.6, 125.6, 125.0, 124.0 (d, *J* = 12.3 Hz), 99.7 (d, *J* = 170.8 Hz), 68.8 (d, *J* = 25.0 Hz), 23.9 (d, *J* = 25.6 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -146.46 (s); HPLC analysis: Daicel Chiralpak AS-H, flow rate =1 ml/min, λ=280 nm, hexane/iso-propanol = 95:5, (*R*)-**4e**: 86% *ee*; $[\alpha]_D^{25}$ = 5.1 (c = 1.30, $CHCl_3$), retention time: 17.5 min (major) and 21.3 min (minor); (*S*)-**4e**: 69% *ee*; $[\alpha]_D^{25}$ = -3.3 (c = 1.73, $CHCl_3$), retention time: 17.4 min (minor) and 21.2 min (major); The spectroscopic data for **4e** matched those described in the literature.[7]

2-fluoro-2-(naphthalen-2-yl)propan-1-ol (4f): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4f** (58.7 mg, 96%) and (*S*)-**4f** (51.4 mg, 84%) as white solid: IR (thin film, cm^{-1}) 3377(br), 2984, 2930, 1601, 1507, 1455, 1379, 1194, 1050, 747; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.79 (m, 4 H), 7.55 – 7.48 (m, 2 H), 7.45 (dd, *J* = 8.7, 1.6 Hz, 1 H), 4.03 – 3.73 (m, 2 H), 2.00 (s, 1 H), 1.80 (d, *J* = 22.6 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0 (d, *J* = 21.5 Hz), 133.2, 132.9, 128.4, 128.3, 127.7, 126.6, 126.4, 123.8, 123.7, 122.6 (d, *J* = 8.4 Hz), 98.2 (d, *J* = 172.5 Hz), 69.6 (d, *J* = 25.2 Hz), 23.4 (d, *J* = 24.7 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -156.55 (s); HPLC analysis: Daicel Chiralpak OD-H, flow rate =1.0 ml/min, λ=210 nm, hexane/iso-propanol = 97:3, (*R*)-**4f**: 85% *ee*; $[\alpha]_D^{25}$ = -14.2 (c = 1.95, $CHCl_3$), retention time: 20.8 min (minor) and 24.8 min (major); (*S*)-**4f**: 88% *ee*; $[\alpha]_D^{25}$ = 14.7 (c = 2.00, $CHCl_3$), retention time: 20.6 min (major) and 24.6 min (minor); The spectroscopic data for **4f** matched those described in the literature.[7]

2-fluoro-2-(4-nitrophenyl)propan-1-ol (4g): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 2:1) to give (*R*)-**4g** (50.2 mg, 84%)

and (*S*)-**4g** (48.9 mg, 82%) as yellow oil: IR (thin film, cm^{-1}) 3443(br),2928, 1607, 1521, 1456, 1409, 1186, 1098, 1054, 755; ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.5 Hz, 2 H), 7.54 (d, *J* = 8.8 Hz, 2 H), 3.93 – 3.76 (m, 2 H), 2.00 (t, *J* = 6.7 Hz, 1 H), 1.71 (d, *J* = 22.5 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.9 (d, *J* = 22.1 Hz), 147.7, 125.8 (d, *J* = 9.8 Hz), 123.8 (d, *J* = 1.5 Hz), 97.7 (d, *J* = 175.1 Hz), 69.2 (d, *J* = 24.9 Hz), 23.4 (d, *J* = 24.5 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -157.51 (s); HPLC analysis: Daicel Chiralpak OD-H, flow rate =1.0 ml/min, λ=210 nm, hexane/iso-propanol = 95:5, (*R*)-**4g**: 83% *ee*; $[\alpha]_D^{25}$ = -15.4 (c = 1.90, $CHCl_3$), retention time: 10.6 min (minor) and 11.8 min (major); (*S*)-**4g**: 87% *ee*; $[\alpha]_D^{25}$ = 17.8 (c = 2.60, $CHCl_3$), retention time: 10.6 min (major) and 11.7 min (minor); The spectroscopic data for **4g** matched those described in the literature.[7]

2-(2-bromophenyl)-2-fluoropropan-1-ol (4h): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4h** (55.9 mg, 80%) and (*S*)-**4h** (52.4 mg, 75%) as yellow oil: IR (thin film, cm^{-1}) 3373(br), 2931, 2873, 1469, 1432, 1375, 1274, 1041, 1732; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.60 (d, *J* = 7.9 Hz, 1 H), 7.40 – 7.33 (m, 1 H), 7.17 (td, *J* = 7.8, 1.6 Hz, 1 H), 4.19 (dddd, *J* = 23.8, 20.1, 12.6, 6.9 Hz, 2 H), 1.85 (d, *J* = 24.4 Hz, 3 H), 1.81 (s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ140.3 (d, *J* = 22.0 Hz), 135.0 (d, *J* = 2.2 Hz), 129.6, 127.9 (d, *J* = 17.2 Hz), 127.8, 118.6 (d, *J* = 5.2 Hz), 99.1 (d, *J* = 173.1 Hz), 67.0 (d, *J* = 23.4 Hz), 21.8 (d, *J* = 25.1 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -147.05 (s); HRMS (EI-TOF) m/z: $[M]^+$ Calcd for $C_9H_{10}BrFO$ 231.9899, 233.9879; Found 231.9901, 233.9878; HPLC analysis: Daicel Chiralpak OJ-H, flow rate =1.0 ml/min, λ=210 nm, hexane/iso-propanol = 97:3, (*R*)-**4h**: 74% *ee*; $[\alpha]_D^{25}$ = - 0.2 (c = 1.00, $CHCl_3$), retention time: 16.1 min (minor) and 17.2 min (major); (*S*)-**4h**: 78% *ee*; $[\alpha]_D^{25}$ = 0.4 (c = 1.75, $CHCl_3$), retention time: 16.0 min (major) and 17.1 min (minor).

2-fluoro-2-(*p*-tolyl)propan-1-ol (4i): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4i** (45.3 mg, 90%) and (*S*)-**4i** (40.8 mg, 81%) as colorless oil: IR (thin film, cm^{-1}) 3374 (br), 2984, 2924, 1615, 1515, 1455, 1378, 1189, 1052, 772; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 2 H), 7.19 (d, *J* = 8.2 Hz, 2 H), 3.93 – 3.62 (m, 2 H), 2.35 (s, 3 H), 1.77 (ddd, *J* = 8.1, 5.6, 1.1 Hz, 1 H), 1.69 (d, *J* = 22.6 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ138.7 (d, *J* = 21.8 Hz), 137.8, 129.3 (d, *J* = 1.1 Hz), 124.6 (d, *J* = 9.0 Hz), 98.0 (d, *J* = 171.7 Hz), 69.8 (d, *J* = 25.3 Hz), 23.3 (d, J = 24.6 Hz), 21.2; ^{19}F NMR (377 MHz, $CDCl_3$) δ -156.31 (d, *J* = 6.0 Hz); HPLC analysis: Daicel Chiralpak AD-H, flow rate =1.0 ml/min, λ=210 nm, hexane/iso-propanol = 95:5, (*R*)-**4i**: 85% *ee*; $[\alpha]_D^{25}$ = - 12.8 (c = 1.80, $CHCl_3$), retention time: 12.9 min (minor) and 15.1 min (major); (*S*)-**4i**: 84% *ee*; $[\alpha]_D^{25}$ = 11.5 (c = 1.65, $CHCl_3$), retention time: 12.9 min (major) and 15.1 min (minor); The spectroscopic data for **4i** matched those described in the literature.[7]

2-fluoro-2-(*m*-tolyl)propan-1-ol (4j): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4j** (41.3 mg, 82%) and (*S*)-**4j** (44.3 mg, 88%) as colorless oil: IR (thin film, cm^{-1}) 3384(br), 2984, 2866, 1609, 1489, 1455, 1378, 1120, 1053, 785; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (t, *J* = 7.9 Hz, 1 H), 7.15 (dd, *J* = 15.6, 7.9 Hz, 3 H), 3.79 (ddd, *J* = 37.5, 20.5, 12.3 Hz, 2 H), 2.37 (d, *J* = 5.6 Hz, 3 H), 1.90 (s, 1 H), 1.68 (d, *J* = 22.7 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δδ 141.6 (d, *J* = 21.3 Hz), 138.3, 128.7,128.5, 125.2 (d, *J* = 9.3 Hz), 121.6 (d, *J* = 9.2 Hz), 98.0 (d, *J* = 172.2 Hz), 69.7 (d, *J* = 25.2 Hz), 23.3 (d, *J* = 24.7 Hz), 21.7; ^{19}F NMR (377 MHz, $CDCl_3$) δ -156.91 (s); HPLC analysis: Daicel Chiralpak AS-H, flow rate =1.0 ml/min, λ=210 nm, hexane/iso-propanol = 95:5, (*R*)-**4j**: 84% *ee*; $[\alpha]_D^{25}$ = - 8.4 (c = 1.10, $CHCl_3$), retention time: 8.8 min (minor) and 9.5 min (major); (*S*)-**4j**: 87% *ee*; $[\alpha]_D^{25}$ = 8.6 (c = 1.75, $CHCl_3$), retention time: 8.8 min (major) and 9.5 min (minor); The spectroscopic data for **4j** matched those described in the literature.[7]

2-fluoro-2-(*o*-tolyl)propan-1-ol (4k): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4k** (14.1 mg, 28%) and (*S*)-**4k** (20.2 mg, 40%) as colorless oil: IR (thin film, cm^{-1}) 3365(br), 2964, 2931, 1490, 1457, 1381, 1100, 1011, 758; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 1 H), 7.23 – 7.16 (m, 3 H), 3.94 (dddd, *J* = 23.2, 20.7, 12.5, 6.9 Hz, 2 H), 2.48 (d, *J* = 3.7 Hz, 3 H), 1.85 – 1.79 (m, 1 H), 1.75 (d, *J* = 23.0 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ139.0 (d, *J* = 20.3 Hz), 135.4, 132.7, 128.2, 126.1 (d, *J* = 1.7 Hz), 125.9 (d, *J* = 11.8 Hz), 99.5 (d, *J* = 171.4 Hz), 68.5 (d, *J* = 24.7 Hz), 23.2 (d, *J* = 25.6 Hz), 21.8 (d, *J* = 7.5 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -150.65 (s); HPLC analysis: Daicel Chiralpak AS-H, flow rate =1.0 ml/min, λ=210 nm, hexane/iso-propanol = 98:2, (*R*)-**4k**: 86% *ee*; $[\alpha]_D^{25}$ = - 1.4 (c = 1.20, $CHCl_3$), retention time: 15.1 min (minor) and 16.7 min (major); (*S*)-**4k**: 75% *ee*; $[\alpha]_D^{25}$ = 0.5 (c = 1.35, $CHCl_3$), retention time: 14.9 min (major) and 16.5 min (minor); The spectroscopic data for **4k** matched those described in the literature.[7]

2-([1,1'-biphenyl]-4-yl)-2-fluoropropan-1-ol (4m): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4m** (57.3 mg, 83%) and (*S*)-**4m** (49.7 mg, 72%) as white solid: IR (thin film, cm^{-1}) 3361 (br), 2918, 2850, 1488, 1403, 1258, 1051, 726; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 10.0, 7.9 Hz, 4 H), 7.45 (dd, *J* = 7.7, 5.7 Hz, 4 H), 7.36 (t, *J* = 7.3 Hz, 1 H), 3.98 – 3.70 (m, 2 H), 1.87 (s, 1 H), 1.75 (d, *J* = 22.6 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ140.9 (d, *J* = 24.3 Hz), 140.7, 140.5, 129.0, 127.6, 127.4, 127.3, 125.1 (d, *J* = 9.2 Hz), 98.0 (d, *J* = 172.2 Hz), 69.7 (d, *J* = 25.2 Hz), 23.4 (d, *J* = 24.7 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -156.79 (s); HPLC analysis: Daicel Chiralpak AD-H, flow rate =1 ml/min, λ=210 nm, hexane/*iso*-propanol = 95:5, (*R*)-**4m**: 90% *ee*; $[\alpha]_D^{25}$ = -19.7 (*c* = 0.40, $CHCl_3$), retention time: 17.6 min (major) and 21.0 min (minor); (*S*)-**4m**: 87% *ee*; $[\alpha]_D^{25}$ = 16.6 (*c* = 1.60, $CHCl_3$), retention time: 17.6 min (minor) and 20.9 min (major); The spectroscopic data for **4m** matched those described in the literature.[7]

2-(3-bromophenyl)-2-fluoropropan-1-ol (4n): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4n** (58.2 mg, 84%) and (*S*)-**4n** (52.6 mg, 76%) as yellow oil: IR (thin film, cm^{-1}) 3360 (br), 2985, 2927, 1596, 1568, 1477, 1417, 1121, 1053, 784; ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 (t, *J* = 2.8 Hz, 1 H), 7.45 (dt, *J* = 7.0, 1.8 Hz, 1 H), 7.30 – 7.24 (m, 2 H), 3.89 – 3.68 (m, 2 H), 1.92 (t, *J* = 6.8 Hz, 1 H), 1.67 (d, *J* = 22.6 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ144.0 (d, *J* = 22.0 Hz), 131.1, 130.2, 127.9 (d, *J* = 10.3 Hz), 123.3 (d, *J* = 9.1 Hz), 122.9, 97.4 (d, *J* = 174.0 Hz), 69.5 (d, *J* = 25.0 Hz), 23.3 (d, *J* = 24.6 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -157.13 (s); HPLC analysis: Daicel Chiralpak AS-H, flow rate =1.0 ml/min, λ=210 nm, hexane/iso-propanol = 95:5, (*R*)-**4n**: 85% *ee*; $[\alpha]_D^{25}$ = - 7.4 (c = 1.20, $CHCl_3$), retention time: 10.7 min (minor) and 12.1 min (major); (*S*)-**4n**: 85% *ee*; $[\alpha]_D^{25}$ = 7.7 (c = 1.85, $CHCl_3$), retention time: 10.6 min (major) and 12.1 min (minor); The spectroscopic data for **4n** matched those described in the literature.[7]

2-fluoro-2-phenylbutan-1-ol (4o): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4o** (40.8 mg, 81%) and (*S*)-**4o** (41.3 mg, 82%) as colorless oil: IR (thin film, cm^{-1}) 3377 (br), 2973, 2934, 1496, 1448, 1340, 1146, 1058, 1023, 759; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 (t, *J* = 7.6 Hz, 2 H), 7.35 – 7.28 (m, 3 H), 3.97 – 3.68 (m, 2 H), 2.25 – 2.06 (m, 1 H), 1.99 – 1.82 (m, 1 H), 1.75 (t, *J* = 6.8 Hz, 1 H), 0.82 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ139.9 (d, *J* = 21.9 Hz), 128.6 (d, *J* = 1.7 Hz), 127.8, 125.0 (d, *J* = 10.1 Hz), 100.5 (d, *J* = 175.6 Hz), 68.9 (d, *J* = 24.6 Hz), 29.1 (d, *J* = 23.5 Hz), 7.3 (d, *J* = 5.0 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -170.41 (s); HPLC analysis: Daicel Chiralpak OJ-H, flow rate =1.0 ml/min, λ=210 nm, hexane/*iso*-propanol = 95:5, (*R*)-**4o**: 60% *ee*; $[\alpha]_D^{25}$ = - 0.4 (*c* = 1.70, $CHCl_3$), retention time: 16.5 min (minor) and 21.6 min (major); (*S*)-**4o**: 69% *ee*; $[\alpha]_D^{25}$ = 1.76 (*c* = 1.65, $CHCl_3$), retention time: 16.3 min (major) and 21.9 min (minor); The spectroscopic data for **4o** matched those described in the literature.[7]

2-fluoro-1,2,3,4-tetrahydronaphthalene-1-ol (4p): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4p** (28.1 mg, 52%) and (*S*)-**4p** (29.7 mg, 55%) as colorless oil: IR (thin film, cm^{-1}) 3391(br), 2937, 2870, 1489, 1452, 1339, 1202, 1013, 728; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 – 7.42 (m, 1 H), 7.28 – 7.20 (m, 2 H), 7.13 (d, *J* = 6.6 Hz, 1 H), 3.97 (t, *J* = 12.2 Hz, 1 H), 3.71 (ddt, *J* = 28.3, 12.5, 4.3 Hz, 1 H), 2.91 – 2.79 (m, 1 H), 2.80 – 2.67 (m, 1 H), 2.40 (tdd, *J* = 13.6, 7.4, 3.1 Hz, 1 H), 2.11 (d, *J* = 4.3 Hz, 1 H), 2.09 – 1.99 (m, 1 H), 1.99 – 1.90 (m, 1 H), 1.86 – 1.75 (m, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ138.3 (d, *J* = 4.0 Hz), 135.0 (d, *J* = 19.7 Hz), 129.0, 128.8 (d, *J* = 2.5 Hz), 126.7 (d, *J* = 5.0 Hz), 126.4 (d, *J* = 1.6 Hz), 95.9 (d, *J* = 171.1 Hz), 67.9 (d, *J* = 29.6 Hz), 30.1 (d, *J* = 21.2 Hz), 29.4 (d, *J* = 1.3 Hz), 20.1 (d, *J* = 7.2 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -143.86 (s); HRMS (APCI-orbitrap) m/z: $[M + H]^+$ Calcd for $C_{11}H_{14}FO$ 181.1023; Found 181.1011; HRMS (APCI) calcd for $C_{11}H_{14}FO^+$: 181.1023, found 181.1011; HPLC analysis: Daicel Chiralpak AS-H, flow rate =1 ml/min, λ=210 nm, hexane/iso-propanol = 95:5, (*R*)-**4p**: 86% *ee*; $[\alpha]_D^{25}$ = -18.3 (c = 0.95, $CHCl_3$), retention time: 16.0 min (major) and 19.8 min (minor); (*S*)-**4p**: 90% *ee*; $[\alpha]_D^{25}$ = 25.6 (c = 1.05, $CHCl_3$), retention time: 16.0 min (minor) and 19.7 min (major).

2-fluoro-3-(4-isopropylphenyl)-2-methylpropan-1-ol (4q): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4q** (39.1 mg, 62%) and (*S*)-**4q** (35.9 mg, 57%) as colorless oil: IR (thin film, cm^{-1}) 3365(br), 2959, 2927, 1512, 1460, 1418, 1381, 1050, 770; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (s, 4 H), 3.58 (d, *J* = 19.4 Hz, 2 H), 2.99 (s, 1 H), 2.93 (t, *J* = 3.7 Hz, 1 H), 2.92 – 2.83 (m, 1 H), 1.79 (s, 1 H), 1.26 (dd, *J* = 14.4, 12.7 Hz, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.4, 133.3, 130.4, 126.5, 97.5 (d, *J* = 170.0 Hz), 67.7 (d, *J* = 23.9 Hz), 42.1 (d, *J* = 23.0 Hz), 33.9, 24.2, 21.1 (d, *J* = 23.8 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -154.23 (s); HPLC analysis: Daicel Chiralpak OJ-H, flow rate =1.0 ml/min, λ=210 nm, hexane/iso-propanol = 97:3,

(*R*)-**4q**: 52% *ee*, retention time: 9.4 min (minor) and 10.6 min (major); (*S*)-**4q**: 27% *ee*, retention time: 9.4 min (major) and 10.6 min (minor); The spectroscopic data for **4q** matched those described in the literature.[8]

2-Ethyl-2-fluorohexan-1-ol (4r): Following the procedure (A and B), the crude mixture was purified by silica gel column chromatography (hexane : diethyl ether = 4:1) to give (*R*)-**4r** (11.1 mg, 25%) and (*S*)-**4r** (5.3 mg, 12%) as colorless oil: IR (thin film, cm^{-1}) 3391(br), 2873, 1054, 748; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (dd, *J* = 20.5, 6.2 Hz, 2 H), 1.75 – 1.57 (m, 4 H), 1.43 (s, 1 H), 1.39 – 1.22 (m, 4 H), 0.96 – 0.84 (m, 6 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 99.9 (d, *J* = 168.6 Hz), 66.3 (d, *J* = 24.1 Hz), 32.9 (d, *J* = 22.4 Hz), 26.4 (d, *J* = 23.3 Hz), 25.4 (d, *J* = 6.7 Hz), 23.3, 14.1, 7.7 (d, *J* = 7.9 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -161.31 (s); GC analysis: CYCLOSIL-B, isotherm 110 ^{o}C, N_2, (*R*)-**4r**: 7% *ee*; retention time: 26.7 min (major) and 28.2 min (minor); (*S*)-**4r**: 0 *ee*.; retention time: 26.7 min and 28.2 min. The spectroscopic data for **4r** matched those described in the literature.[6]

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Supporting Information available: ^{1}H and ^{13}C, ^{19}F NMR spectra, HPLC chart for the products. This material is available free of charge via the Internet at http://pubs.acs.org.

REFERENCES

1. For related publications, see: (a) Muller, K.; Faeh, C.; Diederich, F. *Science.* **2007**, *317*, 1881. (b) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev*. **2008**, *37*, 320. (c) Hiyama, T.; Shimizu, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 214. (d) Mikami, K.; Itoh,Y.; Yamamaka,Y. M. *Chem. Rev*. **2004**, *104*, 1. (e) Arimitsu, S.; Nakasone, M. *J. Org. Chem.* **2016**, *81*, 6707. (f) Arimitsu, S.; Yonamine, T.; Higashi, M. *ACS Catal.* **2017**, *7*, 4736. (g) Yang, J. D.; Wang, Y.; Xue, X. S.; Cheng, J. P. *J. Org. Chem.* **2017**, *82*, 4129.

(h) Li, Y.; Jiang, X.; Zhao, C.; Fu, X.; Xu, X.; Tang, P. *ACS Catal.* **2017**, *7*, 1606.

2. For recent reviews on asymmetric fluorination reactions, see: (a) Champagne, P. A.; Desroches, J.; Hamel, J.-D.; Vandamme, M.; Paquin, J.-F. *Chem. Rev.* **2015**, *115*, 9073. (b) Furuya, T.; Kamlet, A. S.; Ritter, T. *Nature*. **2011**, *473*, 470. (c) Yang, X, Wu, T.; Phipps, R. J.; Toste, F. D. *Chem. Rev.* **2015**, *115*, 826. (d) Britton, R.; Kang, B. *Nat. Prod. Rep.* **2013**, *30*, 227. (e) Smith, A. M. R.; Hii, K. K. *Chem. Rev.* **2011**, *111*, 1637. (f) Lectard, S.; Hamashima, Y.; Sodeoka, M. *Adv. Synth. Catal*. **2010**, *352*, 2708. (g) Lin, J. -H.; Xiao, J. -C. *Tetrahedron Lett.* **2014**, *55*, 6147. (h) Wang, J.; Sánchez-Roselló, M.; Aceña, J. L.; del Pozo, C.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. *Chem. Rev.* **2014**, *114*, 2432. (i) Bizet, V.; Besset, T.; Ma, J.-A.; Cahard, D. *Current Topics in Medicinal Chemistry.* **2014**, *14*, 901. (j) Buckingham, F.; Gouverneur, V. *Chem. Sci.* **2016**, *7*, 1645. (k) Zhou, Y.; Wang, J.; Gu, Z.; Wang, S.; Zhu, Wei.; Aceña, J. L.; Soloshonok, V. A.; Izawa, K.; Liu, H. *Chem. Rev.* **2016**, *116*, 422.

3. For pioneering examples, see: (a) Marigo, M.; Fielenbach, D., Braunton, A.; Kjœrsgaard, A.; Jørgensen, K. A. *Angew. Chem., Int. Ed*. **2005**, *44*, 3703. (b) Steiner, D. D.; Mase, N.; Barbas III, C. F. *Angew. Chem., Int. Ed.* **2005**, *44*, 3706. (c) Beeson, T. D.; MacMillan, D. W. C. *J. Am. Chem. Soc*. **2005**, *127*, 8826. (d) Enders, D.; Hüttle, M. R. *Synlett.* **2005**, 991.

4. For recent enantioselective fluorination of linear aldehydes, see: (a) Hu, X.; Lawer, A.; Peterson, M. B.; Iranmanesh, H.; Ball, G. E.; Hunter, L. *Org. Lett*. **2016**, *18*, 662. (b) Li, F.; Wu, Z.; Wang, J. *Angew. Chem., Int. Ed*. **2015**, *54*, 656. (c) Dong, X.; Yang, W.; Hu, W.; Sun J. *Angew. Chem., Int. Ed.* **2015**, *54*, 660.

5. Sánchez, D.; Bastida, D.; Burés, J.; Isart, C.; Pineda, O.; Vilarrasa, J. *Org. Lett*. **2012**, *14*, 536.

6. Brandes, S; Niess, B.; Bella, M.; Prieto, A.; Overgaard, J.; Jørgensen, K. A. *Chem. Eur. J.* **2006**, *12*, 6039.

7. Witten, M. R.; Jacobsen, E. N. *Org. Lett.* **2015**, *17*, 2772.

8. Shibatomi, K.; Kitahara, K.; Okimi, T.; Abe, Y.; Iwasa, S. *Chem. Sci*. **2016**, *7*, 1388.

9. Zhang, L.; Fu, N.; Luo, S. *Acc. Chem. Res.* **2015**, *48*, 986.

10. You, Y.; Zhang, L.; Luo, S. *Chem. Sci*. **2017**, *8*, 621.

11. For recent reviews on switching selectivity, see: (a) Zanoni, G.; Castronovo, F.; Franzin, M..; Vidari, G.; Giannini, E. *Chem. Soc. Rev*. **2003**, *32*, 115. (b) *Comprehensive Asymmetric Catalysis;* Jacobsen, E., Ed.; Springer: Berlin, 1999. (c) *Catalytic Asymmetric Synthesis;* Ojima. I., Ed.; Wiley-VCH: New York, 2000. (d) Blanco V.; Leigh, D. A.; Marcos, V. *Chem. Soc. Rev*. **2015**, *44*, 5341. (e) Jiang, X.; Wang, R. *Chem. Rev.* **2013**, *113*, 5515. (f) Tanaka, T.; Hayashi, M. *Synthesis*. **2008**, 3361. (g) Bartók, M. *Chem. Rev*. **2010**, *110*, 1663. (h) Escorihuela, J.; Burgueteand, M. I.; Luis, S. V. *Chem. Soc. Rev*. **2013**, *42*, 5595.

12. For organocatalytic enantioselectivity switch, see: (a) Sohtome, Y.; Tanaka, S.; Takada, K.; Yamaguchi, T.; Nagasawa, K. *Angew. Chem., Int. Ed*. **2010**, *49*, 9254. (b) Garzan, A.; Jaganathan, A.; Salehi Marzijarani, N.; Yousefi, R.; Whitehead, D. C.; Jackson, J. E.; Borhan, B. *Chem. Eur. J*. **2013**, *19*, 9015. (c) Moteki, S. A.; Han, J.; Arimitsu, S.; Akakura, M.; Nakayama, K.; Maruoka, K. *Angew. Chem., Int. Ed*. **2012**, *51*, 1187. (d) Fukata, Y.; Asano, K.; Matsubara, S. *J. Am. Chem. Soc*. **2013**, *135*, 12160.

13. Fu, J.-Y.; Xu, X.-Y.; Li, Y.-C.; Huang, Q.-C.; Wang, L.-X. *Org. Biomol. Chem.* **2010**, *8*, 4524.