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Nucleophilic monofluoroalkylation with fluorinated phosphonium salt toward carbonyl and imine compounds

Xian-Liang Zeng[a,b], Zu-Yong Deng[b], Can Liu[b], Gang Zhao[b], Jin-Hong Lin[b,*], Xing Zheng[a,*], Ji-Chang Xiao[b,*]

[a] Institute of Pharmacy and Pharmacology, Hunan Province Cooperative Innovation Center for Molecular Target New Drug Study, University of South China, 28 Western Changsheng Road, Hengyang, Hunan, 421001, China
[b] Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, University of Chinese Academy of Sciences, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China

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ABSTRACT

A fluorinated substituent on the positive phosphorus in phosphonium salt [$Ph_3P^+CF(Me)CO_2Et\ Br^-$] was found to be able to act as a nucleophile to realize monofluoroalkylation of aldehydes, ketones and imines.

1. Introduction

The past decades have witnessed the significant advances in the chemistry of phosphonium salts. Phosphonium salts can act as Lewis acid organocatalysts [1–5], phase-transfer catalysts [6–12], phosphonium ylide precursors [13–17], etc., and therefore have been widely applied to a variety of organic transformations. These synthetic utilities arise from the electrophilicity of the cation. The positive phosphorus is a strong electrophile and can also enhance the electrophilicity of its substituents by an inductive effect. However, we recently discovered that the substituent on the phosphorus can be turned into a nucleophile to realize the construction of C—C bond [18,19], which opens up new avenues to find applications of phosphonium salts. We disclosed that various phosphonium salts could be used as nucleophilic arylation [18] and difluoromethylation [19] reagents in the presence of cesium carbonate. This unprecedented finding stimulates our further development of their applications, and the nucleophilic monofluoroalkylation of aldehydes, ketones and imines with fluorinated phosphonium salt promoted by cesium carbonate was realized to give α-fluoro-β-hydroxy (or −β-amino) esters, which may show biological activities and are important precursors for the preparation of monofluorinated analogues of natural products [20,21].

As the incorporation of fluorine atom into molecules may lead to profound modifications of their physicochemical properties, significant efforts have been directed towards the exploration of efficient methods for fluorine incorporation. A variety of fluorination strategies including nucleophilic [22–26], electrophilic [27–31], photocatalyzed [32–38], transition-metal-catalyzed [23,39–43] and enzymatic [44] fluorination have been well established. Besides fluorination protocols, the conversion of easily available fluorinated building blocks may also serve as a mild alternative for fluorine incorporation [45–54]. Traditionally, α-fluoro-β-hydroxy (or −β-amino) esters are synthesized via Aldol [55–59] (or Mannich) [60,61] or Reformatsky [62–65] reactions by using α-fluoroesters as building blocks. Both the Aldol and Mannich reactions may require strong basic reaction conditions or tedious procedure to produce the enolate intermediates from α-fluoroesters. The Reformatsky reaction usually needs to be promoted by moisture sensitive reagents or proceeds under heating conditions, or may not be applicable to both of carbonyl compounds and imines. We found that the nucleophilic monofluoroalkylation with fluorinated phosphonium salt occurred smoothly at room temperature. The preliminary results are described herein.

* Corresponding authors.
E-mail addresses: jlin@sioc.ac.cn (J.-H. Lin), zhengxing5018@yahoo.com (X. Zheng), jchxiao@sioc.ac.cn (J.-C. Xiao).

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2. Results and discussion

Since phosphonium salt **2′** ($Ph_3P^+CFHCO_2Et\ Br^-$) could be easily obtained by quaternization of Ph_3P with $BrCFHCO_2Et$ (see experimental section), we firstly investigated the monofluoroalkylation of aldehyde **1a** with this phosphonium salt promoted by cesium carbonate (Scheme 1). Disappointingly, Wittig olefination products (*Z*- and *E*-isomers) were produced as the major products and no monofluoroalkylation product **3a'** was observed. Apparently, the generation of phosphonium ylide ($Ph_3P^+CF^-CO_2Et$) from salt **2′** is the reason for the Wittig olefination reaction. Therefore, the α-proton in salt **2′** was replaced by a methyl group and the new phosphonium salt [salt **2**, $Ph_3P^+CF(Me)CO_2Et\ Br^-$] was then investigated in monofluoroalkylation.

Since we have previously shown that Cs_2CO_3 could well promote the nucleophilic addition of a substituent group in phosphonium salts to electrophiles [18,19], the effect of Cs_2CO_3 was firstly examined in our initial attempts at monofluoroalkylation of aldehyde **1a** with phosphonium salt **2** at room temperature. To our delight, the desired product was obtained in 59% yield (Table 1, entry 1). A variety of other promoters were screened, but no higher yield was obtained (Table 1, entries 2–9). A brief survey of the reaction solvents revealed that THF was the suitable choice (Table 1, entries 10–14 vs. entry 1). The molar ratio of the starting materials and reagents was found to have important effects on the transformation (Table 1, entries 15–16). Increasing the ratio of **1a**:**2**: promoter increased the yield to 81% (Table 1, entry 16). The yield was not decreased by increasing the scale of the reaction (Table 1, entry 17).

With the optimized conditions in hand, we then investigate the substrate scope for the monofluoroalkylation with fluorinated phosphonium salt **2** (Scheme 2). The examination of substituent electronic effects for the transformation of aryl aldehydes revealed that electron-withdrawing substituent was favorable (**3a-3 h**), whereas electron-donating substituent would lead to the dramatic decrease in the yield (**3i**). Heteroaryl aldehyde was reactive towards monofluoroalkylation under the optimized conditions (**3j**). The conversion of aliphatic aldehyde such as capraldehyde (30% yield determined by ^{19}F NMR) was not satisfactory. The transformation was also applicable for enolizable aryl ketones (**3 k-3 m**), but only substrates containing strong-electron-withdrawing substituent could be well converted (**3 k-3 l** vs. **3 m**). Aliphatic ketone such as 4-phenylbutan-2-one was inert and no desired product was observed. The reaction of imine could proceed smoothly to afford the expected product in a good yield (**3 n**). The structures and configurations of the products were confirmed by single crystal X-ray diffraction (**3 j**, **3 l** and **3 n**) [66].

On the basis of the above results and our previous studies on nucleophilic addition with phosphonium salts [18,19], we propose that the mechanism shown in Scheme 3 is plausible. The conversion is promoted by Cs_2CO_3 via its nucleophilic attack at the positive phosphorus in salt **2**. Since a nucleophile prefers to attack along the axial direction and pseudorotation would occur afterwards to place the electronegative substituent in the other axial position [67–70], the attack process would generate a trigonal bipyramidal phosphorus species **Int**, an intermediate which is unstable and would readily undergo decarboxylation to cleave the axial P-CF bond. The cleavage of this bond allows for the nucleophilic addition of the $CF(Me)CO_2Et$ group in **Int** to the substrate. The subsequent hydrolysis furnishes the final product. Considering that cyano (in **3c** in Scheme 2) and ester (in all products) groups remains intact, we believe that the free [$CF(Me)CO_2Et$]$^-$ ion is not produced in this monofluoroalkylation reaction.

3. Conclusions

In summary, we have described the nucleophilic addition of a fluorinated substituent in phosphonium salts to aldehydes, ketones and imines promoted by cesium carbonate. This work represents a novel application of phosphonium salts for the construction of C—C bond. The incorporation of fluorine atom into organic molecules was easily realized by this protocol. The strategy of nucleophilic reaction with phosphonium salts may find synthetic utility in other research areas.

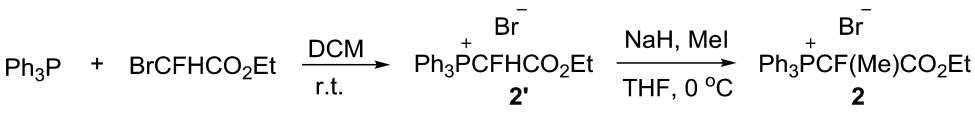
4. Experimental section

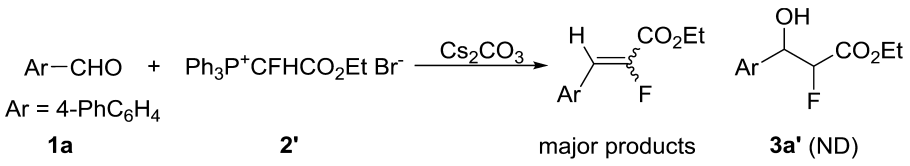
4.1. General information

^1H, ^{13}C, ^{19}F and ^{31}P NMR spectra were detected on a 500 MHz, 400 MHz or 300 MHz NMR spectrometer. Data for ^1H NMR, ^{13}C NMR, ^{31}P NMR and ^{19}F NMR were recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, coupling constant (s) in Hz). Mass spectra were obtained on GC–MS or ESI. High resolution mass data were recorded on a high resolution mass spectrometer in the EI or ESI.

4.2. The procedure for the synthesis of compound *2*

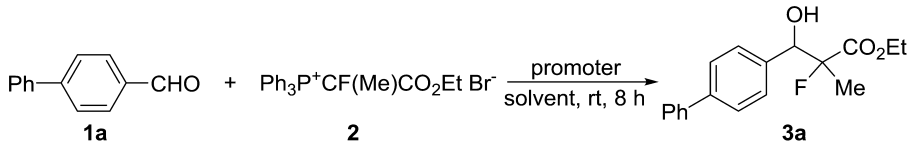
Compound **2'** was prepared according to literature [71]. The solution of triphenylphosphine (286 g, 1.09 mol) and ethyl 2-bromo-2-fluoroacetate (153.6 g, 0.85 mol) in dichloromethane (80 mL) was stirred at room temperature for 3 days. The solvent was removed by concentration under reduced pressure. The crude product was recrystallized with ethyl ether to give a white solid (**2′**, 307.9 g, 81% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 9.61 (dd, *J* = 41.5, 6.0 Hz, 1H), 8.02–7.61 (m, 15H), 4.13–4.01 (m, 2H), 0.96 (t, *J* = 7.1 Hz,





Scheme 1. Unsuccessful monofluoroalkylation with salt **2'**.

Table 1
Screening conditions for monofluoroalkylation[a].



entry	solvent	promoter	ratio[b]	Yield (%)[c]
1	THF	Cs_2CO_3	1:1.5:2	59
2	THF	$CsHCO_3$	1:1.5:2	50
3	THF	HCO_2Cs	1:1.5:2	N.D
4	THF	$Na_2C_2O_4$	1:1.5:2	N.D
5	THF	Na_2CO_3	1:1.5:2	8
6	THF	LiOH	1:1.5:2	N.D
7	THF	KF	1:1.5:2	N.D
8	THF	CsF	1:1.5:2	18
9	THF	AgF	1:1.5:2	41
10	DMF	Cs_2CO_3	1:1.5:2	39
11	CH_3CN	Cs_2CO_3	1:1.5:2	28
12	DMSO	Cs_2CO_3	1:1.5:2	19
13	Cyclohexane	Cs_2CO_3	1:1.5:2	5
14	1,4-Dioxane	Cs_2CO_3	1:1.5:2	37
15	THF	Cs_2CO_3	1:2:2.5	72
16	THF	Cs_2CO_3	1:3:3.5	81
17[d]	THF	Cs_2CO_3	1:3:3.5	83

[a] Reaction conditions: **1a** (0.2 mmol), **2** and promoter in solvent (2 mL).
[b] Molar ratio of **1a**:**2**:promoter.
[c] The yields were determined by ^{19}F NMR.
[d] The scale of the reaction was increased to 0.5 mmol (substrate **1a**).

3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −201.81 (dd, J = 68.2, 41.8 Hz, 1 F). ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.71 (d, J = 67.6 Hz, 1 P).

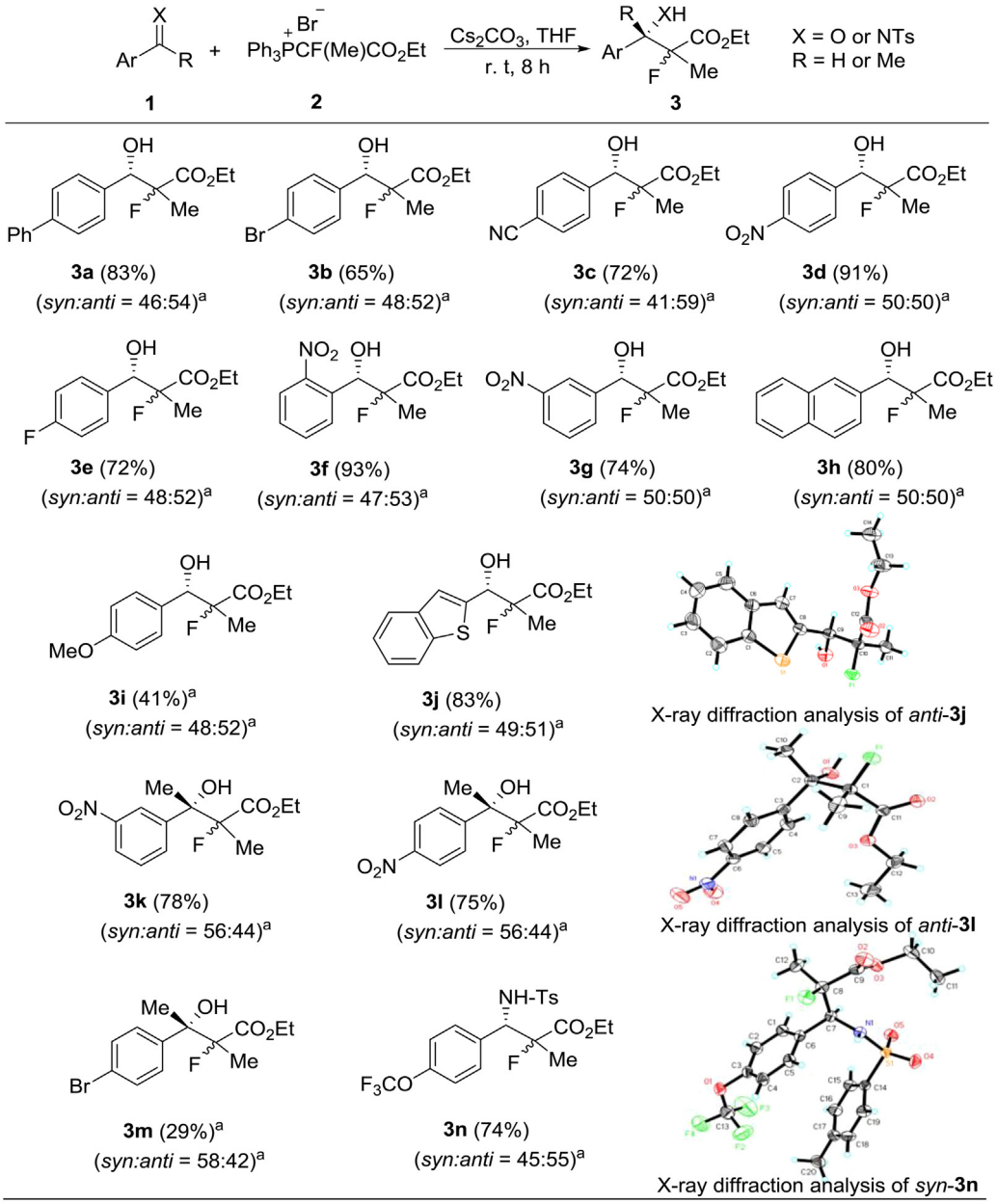
Into the mixture of $Ph_3P^+CFHCO_2Et\ Br^-$ (13.5 g, 30 mmol) and dry THF (60 mL) was added NaH (1.44 g, 36 mmol) at 0 °C under N_2 atmosphere. The resulting mixture was stirred at the same temperature for 10 min. MeI (6 g, 42 mmol) was added and the solution was warmed to room temperature. After 4 h, the reaction was quenched by hydrobromic acid (40%) and the organic layer was extracted with dichloromethane (50 mL, three times). The organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The crude product was recrystallized with dichloromethane and ethyl acetate to give the final product **2** (7 g, 51% yield). White solid. M.P. 150.1–151.5 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.22–7.52 (m, 15 H), 4.18 (q, J = 7.1 Hz, 2 H), 2.26 (dd, J = 23.5, 15.5 Hz, 3 H), 1.05 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −153.24 (dq, J = 79.4, 23.6 Hz, 1F). ^{31}P NMR (162 MHz, $CDCl_3$) δ 30.69 (d, J = 79.7 Hz, 1P). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.88 (dd, J = 22.7, 7.1 Hz), 136.50 (d, J = 3.1 Hz), 134.55 (d, J = 10.1 Hz), 131.07 (d, J = 13.0 Hz), 113.89 (d, J = 84.0 Hz), 95.52 (dd, J = 215.3, 62.9 Hz), 64.84 (s), 23.39 (dd, J = 21.7, 2.8 Hz), 13.59 (s). IR (neat) ν = 3436, 3052, 2986, 2932, 2360, 2341, 1735, 1584, 1482, 1378, 1189, 1163, 1134, 934, 850, 752, 669, 565, 502, 408 cm^{-1}. HRMS (ESI): calcd. for $[C_{23}H_{23}O_2FP]$ $(M\text{-}Br)^+$: 381.1414, found 381.1414.

4.3. The general procedure for nucleophilic monofluoroalkyation

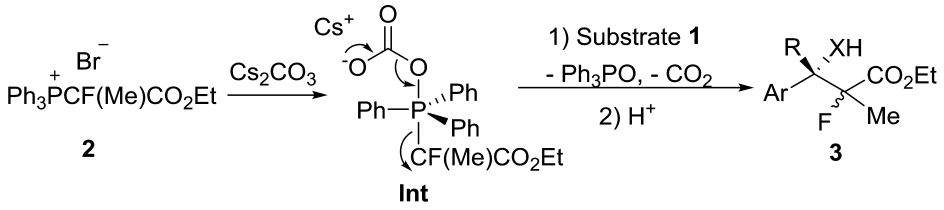
Into a mixture of substrate (0.5 mmol, 1.0 equiv.), phosphonium salt **2** (1.5 mmol, 3.0 equiv.), cesium carbonate (1.75 mmol, 3.5 equiv.) was added THF (4 mL) under N_2 atmosphere. The resulting mixture was stirred at room temperature for 8 h, and was then diluted with CH_2Cl_2 (15 mL) and water (15 mL). The organic phase was separated and washed with water (15 mL, three times), and then dried over Na_2SO_4. After filtration, the solvent was removed by concentration. The residue was subjected to flash column chromatography with petroleum/ethyl acetate as eluent to give the final product.

Ethyl-3-([1,1′-biphenyl]-4-yl)-2-fluoro-3-hydroxy-2-methyl-propanoate (**3a**): 83%, *syn: anti* = 46:54. ***anti*** − **3a**: white solid. M.P.: 107.6–108.6 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.59–7.54 (m, 4 H), 7.47–7.40 (m, 4 H), 7.34 (t, J = 7.3 Hz, 1H), 5.00 (d, J = 16.2 Hz, 1 H), 4.22–4.09 (m, 2 H), 2.96 (s, 1 H), 1.63 (d, J = 22.1 Hz, 3H), 1.18 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −165.04– −165.30 (m, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.88 (d, J = 24.0 Hz), 141.36 (s), 140.65 (s), 136.77 (s), 128.81 (s), 128.01 (s), 127.45 (s), 127.10 (s), 126.87 (s), 96.12 (d, J = 191.0 Hz), 76.03 (d, J = 23.0 Hz), 61.89 (s), 19.46 (d, J = 23.7 Hz), 13.97 (s). IR (neat) ν = 3508, 3055, 3004, 1725, 1485, 1469, 1392, 1308, 1298, 1155, 1130, 875, 859, 747, 721, 702, 670 cm^{-1}. HRMS (EI): calcd. for $[C_{18}H_{19}FO_3]^+$ $[M]^+$: 302.1313, found 302.1314. ***syn*** − **3a**: white solid. M.P.: 117.5–118.2 °C ^1H NMR (400 MHz, $CDCl_3$) δ 7.60–7.55 (m, 4 H), 7.47–7.41 (m, 4 H), 7.34 (t, J = 7.3 Hz, 1 H)., 4.98 (d, J = 21.1 Hz, 1 H), 4.29 (qd, J = 7.1, 0.9 Hz, 2 H), 2.69 (s, 1 H), 1.44 (d, J = 21.7 Hz, 3 H), 1.31 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) −171.05– −171.35 (m, 1 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.13 (d, J = 25.2 Hz), 141.58 (s), 140.54 (s), 136.51 (s), 128.83 (s), 128.25 (d, J = 1.9 Hz), 127.52 (s), 127.11 (s), 127.09 (s), 96.53 (d, J = 193.0 Hz), 77.20 (d, J = 20.9 Hz), 62.07 (s), 20.51 (d, J = 23.5 Hz), 14.11 (s). IR (neat) ν = 3420, 3057, 2982, 1754, 1488, 1447, 1394, 1376, 1304, 1271, 1138, 1108, 1047, 1021, 791, 746, 725, 693, 553 cm^{-1}. HRMS (EI): calcd. for $[C_{18}H_{19}FO_3]^+$ $[M]^+$: 302.1313, found 302.1324.

Ethyl −3-(4-bromophenyl)-2-fluoro-3-hydroxy-2-methylpropanoate (**3b**):65%, *syn: anti* = 48:52. ***anti*** − **3b**: Colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.0 Hz, 2 H), 7.25 (d, J = 8.0 Hz, 2 H), 4.91 (dd, J = 14.8, 3.2 Hz, 1 H), 4.15 (qd, J = 7.1, 2.4 Hz, 2 H), 2.99 (d, J = 3.2 Hz, 1 H), 1.54 (d, J = 22.2 Hz, 3 H), 1.19 (t, J = 7.1 Hz, 3 H).). ^{19}F NMR (376 MHz, $CDCl_3$) δ −164.66 (qd, J = 22.2, 15.4 Hz, 1 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.81 (d, J = 24.0 Hz), 136.63 (s), 131.27 (s), 129.28 (d, J = 2.0 Hz), 122.57 (s), 95.67 (d, J = 191.2 Hz), 75.44 (d, J = 23.4 Hz), 62.03 (s), 19.11 (d, J = 23.6 Hz), 13.97 (s).IR (neat)



Scheme 2. Substrate scope for monofluoroalkylation. Isolated yields. [a]Determined by ^{19}F NMR.



Scheme 3. The proposed reaction mechanism.

ν = 3478, 2924, 2853, 1742, 1446, 1375, 1302, 1284, 1174, 1137, 1071, 936, 840, 801, 735, 524 cm^{-1}. HRMS (EI): calcd. for $[C_{12}H_{14}BrFO_3]^+$ $[M]^+$: 304.0105, found 304.0104. ***syn*** – **3b**: Colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.0 Hz, 2 H), 7.24 (d, J = 8.0 Hz, 2 H), 4.89 (dd, J = 20.3, 5.8 Hz, 1H), 4.15 (qd, J = 7.1, 2.4 Hz, 2 H), 2.79 (br, 1 H), 1.38 (d, J = 22.2 Hz, 3 H), 1.29 (t, J = 7.1 Hz, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −170.89 (p, J = 22.2 Hz, 1 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.90 (d, J = 25.1 Hz), 136.51 (s), 131.52 (s), 129.48 (d, J = 2.1 Hz), 122.80 (s), 96.16 (d, J = 193.3 Hz), 76.76 (d, J = 20.7 Hz), 62.18 (s), 20.44 (d, J = 23.5 Hz), 14.10 (s). IR (neat) ν = 3467, 2924, 2853, 1487, 1438, 1404, 1374, 1301, 1284, 1260, 1174, 935, 840, 801,

723, 695, 541, 524 cm^{-1}. HRMS (EI): calcd. for $[C_{12}H_{14}BrFO_3]^+$ $[M]^+$ 304.0105, found 304.0104.

Ethyl −3-(4-cyanophenyl)-2-fluoro-3-hydroxy-2-methylpropanoate (**3c**): 72%, *syn: anti* = 41:59. ***anti* – 3c**: Colourless oil.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.0 Hz, 2 H), 7.50 (d, J = 8.1 Hz, 2 H), 5.04 (dd, J = 13.4, 4.2 Hz, 1 H), 4.19 (q, J = 7.2 Hz, 2 H), 3.21 (d, J = 4.3 Hz, 1 H), 1.52 (d, J = 22.3 Hz, 3 H), 1.22 (t, J = 7.1 Hz, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −163.48 (qd, J = 22.1, 13.4 Hz, 1 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.79 (d, J = 23.6 Hz), 142.78 (s), 131.85 (s), 128.41 (d, J = 2.2 Hz), 118.58 (s), 112.26 (s), 95.34 (d, J = 192.0 Hz), 75.08 (d, J = 23.9 Hz), 62.25 (s), 18.79 (d, J = 23.5 Hz), 13.98 (s). IR (neat) ν = 3473, 2987, 2230, 1739, 1610, 1505, 1447, 1395, 1174, 1109, 1068, 1019, 952, 857, 788, 770, 751, 572, 448 cm^{-1}. HRMS (ESI): calcd. for $[C_{13}H_{18}FN_2O_3]$ $(M+NH_4)^+$: 269.1296, found 269.1297. ***syn* – 3c**: Colourless oil.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.3 Hz, 2H), 7.50 (d, J = 7.7 Hz, 2H), 4.98 (dd, J = 20.0, 7.1 Hz, 1 H), 4.26 (q, J = 7.1 Hz, 2 H), 2.93 (d, J = 7.1 Hz, 1 H), 1.44 (d, J = 21.8 Hz, 3 H), 1.27 (t, J = 7.1 Hz, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −169.36 (p, J = 21.4 Hz, 1 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.60 (d, J = 24.8 Hz), 142.69 (s), 132.03 (s), 128.51 (d, J = 2.2 Hz), 118.43 (s), 112.52 (s), 95.86 (d, J = 194.0 Hz), 76.63 (d, J = 29.6 Hz), 62.32 (s), 20.50 (d, J = 23.5 Hz), 14.05 (s). IR (neat) ν = 3476, 2852, 2228, 1737, 1445, 1376, 1287, 1260, 1175, 1109, 1018, 937, 852, 801, 557, 422, 414, 402 cm^{-1}. HRMS (ESI): calcd. for $[C_{13}H_{18}FN_2O_3]$ $(M+NH_4)^+$: 269.1296, found 269.1296.

Ethyl −2-fluoro-3-hydroxy-2-methyl-3-(4-nitrophenyl)propanoate (**3d**): 91%, *syn: anti* = 50:50. ***anti* – 3d**: light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.7 Hz, 2 H), 7.57 (d, J = 8.3 Hz, 2 H), 5.11 (dd, J = 12.8, 4.3 Hz, 1 H), 4.21 (q, J = 7.1 Hz, 2 H), 3.24 (d, J = 4.3 Hz, 1 H), 1.53 (d, J = 22.3 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −163.03 (qd, J = 22.3, 12.8 Hz, 1 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.81 (d, J = 23.6 Hz), 147.97 (s), 144.60 (s), 128.59 (d, J = 2.1 Hz), 123.19 (s), 95.23 (d, J = 192.0 Hz), 74.89 (d, J = 24.0 Hz), 62.33 (s), 18.70 (d, J = 23.4 Hz), 13.98 (s). IR (neat) ν = 3495, 2987, 2941, 1739, 1607, 1522, 1607, 1348, 1303, 1175, 1136, 1110, 1068, 1015, 953, 861, 835, 809, 731, 714, 699, 543 cm^{-1}. HRMS (ESI): calcd. for $[C_{12}H_{18}FN_2O_5]$ $(M+NH_4)^+$: 289.1194, found 289.1192. ***syn* – 3d**: light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H), 5.04 (dd, J = 18.9, 7.1 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 3.09 (d, J = 7.0 Hz, 1H), 1.44 (d, J = 21.8 Hz, 3H), 1.28 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −169.21– −169.50 (m,1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.61 (d, J = 24.8 Hz), 148.07 (s), 144.65 (s), 128.75 (d, J = 2.0 Hz), 123.41 (s), 95.85 (d, J = 194.1 Hz), 76.42 (d, J = 21.6 Hz), 62.39 (s), 20.52 (d, J = 23.5 Hz), 14.06 (s). IR (neat) ν = 3482, 3114, 2987, 2923, 2851, 1742, 1607, 1522, 1448, 1376, 1349, 1300, 1264, 1176, 1139, 1152, 1065, 939, 863, 847, 723, 699, 517, 441 cm^{-1}.HRMS (ESI): calcd. for $[C_{12}H_{18}FN_2O_5]$ $(M+NH_4)^+$: 289.1194, found 289.1193.

Ethyl −2-fluoro-3-(4-fluorophenyl)-3-hydroxy-2-methylpropanoate (**3e**): 72%, *syn: anti* = 48:52. ***anti* – 3e**: Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (dd, J = 7.3, 6.1 Hz, 2H), 6.99 (t, J = 8.6 Hz, 2H), 4.90 (d, J = 16.0 Hz, 1H), 4.27–3.94 (m, 2H), 3.06 (s, 1H), 1.54 (d, J = 22.1 Hz, 3H), 1.16 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −113.51 – −113.76 (m,1F), −162.73 – −172.21 (m, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.84 (d, J = 23.9 Hz), 162.80 (d, J = 246.9 Hz), 133.48 (d, J = 2.9 Hz), 129.33 (dd, J = 8.2, 2.1 Hz), 115.05 (d, J = 21.5 Hz), 95.88 (d, J = 191.2 Hz), 75.48 (d, J = 23.1 Hz), 61.92 (s), 19.24 (d, J = 23.7 Hz), 13.94 (s). IR (neat) ν = 3750, 3648, 3480, 3077, 2987, 2942, 1739, 1606, 1558, 1511, 1447, 1375, 1304, 1224, 1159, 1110, 1061, 1061, 956, 846, 821, 788, 762, 734, 580, 551, 474 cm^{-1}. HRMS (EI): calcd. for $[C_{12}H_{14}F_2O_3]^+$ $[M]^+$: 244.0906, found 244.0912. ***syn* – 3e**: Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, J = 8.0, 5.7 Hz, 2H), 7.04 (t, J = 8.6 Hz, 2H), 4.91 (d, J = 20.7 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 2.44 (s, 1H), 1.37 (d, J = 21.7 Hz, 3H), 1.28 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −113.24 – −113.33 (m, 1F), −171.34 (p, J = 21.4 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.02 (d, J = 25.2 Hz), 162.89 (d, J = 246.6 Hz), 133.39 (d, J = 2.7 Hz), 129.55 (dd, J = 8.2, 1.9 Hz), 115.28 (d, J = 21.5 Hz), 96.35 (d, J = 193.0 Hz), 76.67 (d, J = 20.6 Hz), 62.09 (s), 20.39 (d, J = 23.9 Hz), 14.07 (s). IR (neat) ν = 3481, 3077, 2987, 2941, 1742, 1605, 1511, 1448, 1375, 1301, 1225, 1175, 1113, 1059, 1015, 847, 819, 792, 586, 537 cm^{-1}. HRMS (EI): calcd. for $[C_{12}H_{14}F_2O_3]^+$ $[M]^+$: 244.0906, found 244.0907.

Ethyl −2-fluoro-3-hydroxy-2-methyl-3-(2-nitrophenyl)propanoate (3**f**): 93%, *syn: anti* = 47:53. ***anti* – 3f**: light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.9 Hz, 1H), 7.82 (d, J = 8.1 Hz, 1H), 7.62 (t, J = 7.7 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 5.85 (d, J = 13.6 Hz, 1H), 4.22 – 4.06 (m, 2H), 3.29 (s, 1H), 1.55 (d, J = 22.4 Hz, 3H), 1.18 (t, J = 7.1 Hz, 3H).^{19}F NMR (376 MHz, $CDCl_3$) δ −164.65 (qd, J = 22.3, 14.0 Hz 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.67 (d, J = 24.1 Hz), 149.49 (s), 132.70 (s), 131.84 (s), 129.73 (d, J = 3.5 Hz), 129.18 (s), 124.42 (s), 95.59 (d, J = 193.1 Hz), 69.36 (d, J = 22.9 Hz), 62.25 (s), 19.12 (d, J = 24.0 Hz), 13.81 (s). IR (neat) ν = 3494, 2987, 2942, 1739, 1530, 1446, 1355, 1300, 1173, 1136, 1111, 1091, 1058, 1041, 1016, 859, 812, 787, 738, 685, 553 cm^{-1}.HRMS (ESI): calcd. for $[C_{12}H_{18}FN_2O_5]$ $(M+NH_4)^+$: 289.1194, found 289.1193. ***syn* – 3f**: light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.1 Hz, 1H), 7.83 (d, J = 7.9 Hz, 1H), 7.64 (t, J = 8.0 Hz, 1H), 7.47 (t, J = 8.0 Hz, 1H), 5.86 (d, J = 20.1 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.37 (s, 1H), 1.40 (d, J = 22.2 Hz, 3H), 1.27 (t, J = 7.1 Hz, 3H).^{19}F NMR (376 MHz, $CDCl_3$) δ −169.92 (p, J = 21.5 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.56 (d, J = 25.3 Hz), 149.25 (s), 133.18 (s), 132.55 (s), 130.33 (d, J = 4.4 Hz), 129.30 (s), 124.28 (s), 96.58 (d, J = 194.3 Hz), 70.57 (d, J = 20.1 Hz), 62.33 (s), 20.44 (d, J = 23.3 Hz), 14.03 (s). IR (neat) ν = 2923, 1740, 1653, 1636, 1609, 1577, 1558, 1528, 1351, 1296, 1139, 1111, 1057, 1017, 939, 860, 789, 717, 419 cm^{-1}. HRMS (ESI): calcd. for $[C_{12}H_{18}FN_2O_5]$ $(M+NH_4)^+$: 289.1194, found 289.1192.

Ethyl −2-fluoro-3-hydroxy-2-methyl-3-(3-nitrophenyl)propanoate (**3 g**): 74%, *syn: anti* = 50:50. ***anti* – 3 g**: light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 8.15 (dd, J = 8.2, 1.3 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 5.10 (d, J = 13.8 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 3.40 (s, 1H), 1.54 (d, J = 22.2 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −163.66 (qd, J = 22.2, 13.8 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.60 (d, J = 23.9 Hz), 148.02 (s), 139.75 (s), 133.76 (d, J = 2.1 Hz), 129.08 (s), 123.37 (s), 122.67 (d, J = 1.9 Hz), 95.96 (d, J = 191.4 Hz), 74.86 (d, J = 23.9 Hz), 62.35 (s), 18.84 (d, J = 23.4 Hz), 13.97 (s). IR (neat) ν = 3487, 3092, 2987, 2941, 1739, 1532, 1446, 1351, 1303, 1175, 1138, 1110, 1016, 767, 729, 687 cm^{-1}.HRMS (ESI): calcd. for $[C_{12}H_{15}FNO_5]$ $(M+H)^+$: 272.0929, found 272.0928. ***syn*- 3 g**: light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 8.21 – 8.17 (m, 1H). 7.73 (dd, J = 7.7, 1.1 Hz, 1H), δ 7.55 (t, J = 8.0 Hz, 1H), 5.04 (d, J = 18.9 Hz, 1H), 4.30 – 4.23 (m, 2H), 3.15 (s, 1H), 1.45 (d, J = 21.8 Hz, 3H), 1.28 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −169.4(p, J = 21.8 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.60 (d, J = 24.9 Hz), 148.16 (s), 139.75 (s), 133.84 (s), 129.32 (s), 123.56 (s), 122.79 (s), 95.93 (d, J = 193.6 Hz), 76.36 (d, J = 21.7 Hz), 62.40 (s), 20.49 (d, J = 23.4 Hz), 14.05 (s). IR (neat) ν = 3481, 3092, 2987, 2922, 1742, 1532, 1447, 1351, 1298, 1174, 1140, 1113, 1058, 1017, 906, 767, 723, 691, 669, 545 cm^{-1}. HRMS (ESI): calcd. for $[C_{12}H_{18}FN_2O_5]$ $(M+NH_4)^+$: 289.1194, found 289.1192.

Ethyl 2-fluoro-3-hydroxy-2-methyl-3-(naphthalen-2-yl)propanoate (3 **h**): 80%, *syn: anti* = 50:50. ***anti* – 3 h**: Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85-7.76 (m, 4H), 7.52-7.42 (m, 3H), 5.12 (d, J = 16.0 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 2.96 (s, 1H), 1.62 (d, J = 22.2 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −164.31 – −164.71 (m 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.91 (d, J = 24.0 Hz), 135.20 (s), 133.36 (s), 132.93 (s), 128.15 (s), 127.85 (s), 127.66 (s), 126.90 (d, J = 1.3 Hz), 126.28 (s), 126.19 (s), 125.20 (d, J = 2.5 Hz), 96.19 (d, J = 190.9 Hz), 76.33 (d, J = 23.1 Hz), 61.89 (s), 19.45 (d, J = 23.7 Hz), 13.93 (s). IR (neat) ν = 34802, 3052, 2985, 2939, 1739, 1507, 1446, 1373, 1330, 1136, 1122, 1062, 1018, 948, 861,

820, 791, 747, 480 cm^{-1}. HRMS (EI): calcd. for $[C_{16}H_{17}FO_3]^+$ $[M]^+$: 276.1156, found 276.1158. ***syn*** – **3h:** Colourless oil.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.80 (m, 4H). 7.55-7.45 (m, 3H), 5.10 (dd, J = 21.3, 6.1 Hz, 1H), 4.28 (q, J = 7.0 Hz, 2H), 2.91 (d, J = 6.4 Hz, 1H), 1.42 (d, J = 21.7 Hz, 3H), 1.28 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −171.00 (p, J = 21.1 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.20 (d, J = 25.2 Hz), 135.02 (s), 133.39 (s), 132.94 (s), 128.17 (s), 128.13 (s), 127.70 (s), 127.37 (d, J = 1.1 Hz), 126.43 (s), 126.34 (s), 125.24 (d, J = 2.7 Hz), 96.67 (d, J = 193.1 Hz), 77.55 (d, J = 20.6 Hz), 62.09 (s), 20.55 (d, J = 23.5 Hz), 14.10 (s). IR (neat) ν = 3481, 3057, 2984, 2937, 1739, 1653, 1646, 1601, 1540, 1447, 1374, 1269, 1173, 1139, 1111, 1060, 1018, 861, 795, 761, 746, 515, 480 cm^{-1}. HRMS (EI): calcd. for $[C_{16}H_{17}FO_3]^+$ $[M]^+$: 276.1156, found 276.1170.

Ethyl-3-(benzo[b]thiophen-2-yl)-2-fluoro-3-hydroxy-2-methylpropanoate (**3j**): 83%, *syn: anti* = 49:51. ***anti*** – **3j**: white solid, M. P.: 72.5 – 74.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.67 (m, 2H), 7.40- 7.28 (m, 3H), 5.26 (d, J = 20.0 Hz, 1H), δ 4.12 (q, J = 7.0 Hz, 2H), 2.79 (br, 1H), 1.54 (d, J = 21.6 Hz, 3H), 1.29 (t, J = 7.0 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −169.30 (p, J = 21.0 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.72 (d, J = 25.0 Hz), 140.98 (s), 140.10 (d, J = 1.7 Hz), 138.97 (s), 124.74 (s), 124.43 (s), 123.85 (d, J = 1.5 Hz), 123.78 (s), 122.38 (s), 96.15 (d, J = 193.7 Hz), 74.14 (d, J = 22.1 Hz), 62.28 (s), 20.63 (d, J = 23.3 Hz), 14.07 (s). IR (neat) ν = 3566, 3447, 3057, 2984, 2938, 1734, 1458, 1437, 1374, 1304, 1120, 1045, 1015, 949, 861, 748, 727, 709, 418 cm^{-1}. HRMS (EI): calcd. for $[C_{14}H_{15}FO_3S]^+$ $[M]^+$ 282.0720, found 282.0728. ***syn*** – **3j:** colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.67 (m, 2H), 7.50 – 7.31 (m, 3H), 5.29 (d, J = 19.9 Hz, 1H), δ 4.33 (q, J = 6.5 Hz, 2H), 2.98 (s, 1H), 1.58 (d, J = 21.5 Hz, 3H), 1.31 (t, J = 6.5 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −168.99 – −169.32 (m, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.72 (d, J = 27.7 Hz), 140.98 (s), 140.10 (d, J = 1.7 Hz), 138.97 (s), 124.74 (s), 124.43 (s), 123.85 (d, J = 1.5 Hz), 123.78 (s), 122.38 (s), 96.15 (d, J = 193.7 Hz), 74.14 (d, J = 22.1 Hz), 62.28 (s), 20.63 (d, J = 23.3 Hz), 14.07 (s). IR (neat) ν = 3470, 3057, 2985, 2937, 1740, 1457, 1437, 1375, 1304, 1277, 1120, 1051, 1015, 861, 749, 727, 565, 540, 439 cm^{-1}. HRMS (EI): calcd. for $[C_{14}H_{15}FO_3S]^+$ $[M]^+$: 282.0720, found 282.0729.

Ethyl 2-fluoro-3-hydroxy-2-methyl-3-(3-nitrophenyl)butanoate (**3k**): 78%, *syn: anti* = 56:44. ***syn*** – **3k:** light yellow oil.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.18–8.00 (m, 1H), 7.85 (d, J = 8.5 Hz, 1H), 7.49 (t, J = 8.0 Hz, 1H), 4.06 – 3.97 (m, 2H), 3.94 (s, 1H), 1.73 (d, J = 22.9 Hz, 3H), 1.63 (d, J = 1.4 Hz, 3H), 0.98 (t, J = 7.5 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −159.56 (q, J = 22.3 Hz 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.20 (d, J = 23.5 Hz), 148.05 (s), 146.23 (s), 132.27 (d, J = 4.7 Hz), 128.95 (s), 122.57 (s), 121.17 (d, J = 4.0 Hz), 97.00 (d, J = 199.6 Hz), 76.08 (d, J = 22.6 Hz), 62.25 (s), 23.41 (d, J = 2.9 Hz), 19.32 (d, J = 24.0 Hz), 13.73 (s). IR (neat) ν = 3502, 2852, 1735, 1457, 1307, 1232, 1015, 945, 882, 857, 808, 772, 742, 691, 551, 487 cm^{-1}. HRMS (ESI): calcd. for $[C_{13}H_{20}O_5N_2F]$ $(M+NH_4)^+$: 303.1351, found 303.1350. ***anti*** – **3k:** light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), δ 8.19 – 8.12 (m, 1H), 7.87 (d, J = 7.8 Hz, 1H), 7.52 (t, J = 8.0 Hz, 1H), 4.40 – 4.26 (m, 2H), 4.04 (s, 1H), 1.67 (d, J = 1.5 Hz, 3H), 1.35 (d, J = 22.1 Hz, 3H), 1.34 (t, J = 7.4 Hz, 3H).^{19}F NMR (376 MHz, $CDCl_3$) δ −160.82 (q, J = 22.2 Hz 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.73 (d, J = 23.6 Hz), 148.08 (s), 143.52 (s), 133.09 (d, J = 3.5 Hz), 128.72 (s), 122.62 (s), 122.20 (d, J = 3.0 Hz), 96.51 (d, J = 199.0 Hz), 75.55 (d, J = 23.0 Hz), 62.67 (s), 25.36 (d, J = 1.3 Hz), 19.43 (d, J = 23.1 Hz), 14.08 (s). IR (neat) ν = 3420, 2919, 249, 1653, 1558, 1540, 1533, 1457, 1350, 1309, 1199, 1120, 1105, 1055, 1042, 1014, 938, 812, 690, 569, 419 cm^{-1}. HRMS (ESI): calcd. for $[C_{13}H_{20}O_5\ N_2F]$ $(M+NH_4)^+$: 303.1351, found 303.1351.

Ethyl 2-fluoro-3-hydroxy-2-methyl-3-(4-nitrophenyl)butanoate (**3l**): 75%, *syn*: *anti* = 56:44. ***syn*** – **3l:** light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.9 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H), 4.00 (q, J = 7.1 Hz, 2H), 3.94 (s, 1H), 1.73 (d, J = 22.3 Hz, 3H), 1.60 (d, J = 1.2 Hz, 3H), 0.99 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −159.21 (q, J = 22.3 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.30 (d, J = 23.2 Hz), 151.34 (s), 147.29 (s), 127.03 (d, J = 4.6 Hz), 123.06 (s), 96.93 (d, J = 200.4 Hz), 76.32 (d, J = 22.5 Hz), 62.28 (s), 23.34 (d, J = 3.0 Hz), 19.39 (d, J = 24.0 Hz), 13.75 (s). IR (neat) ν = 3481, 3115, 2987, 2918, 2849, 1734, 1717, 1603, 1521, 1457, 1448, 1348, 1306, 1230, 1134, 1099, 1014, 942, 856, 831, 729, 701, 575, 419 cm^{-1}. HRMS (ESI): calcd. for $[C_{13}H_{20}FN_2O_5]$ $(M+NH_4)^+$: 303.1351, found 303.1348. ***anti*** – **3l:** light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 9.0 Hz, 2H), 7.73 (d, J = 9.0 Hz, 2H), δ 4.39 – 4.25 (m, 2H), 4.06 (s, 1H), 1.65 (s, 3H), 1.35(t, J = 7.0 Hz, 3H), 1.34 (d, J = 22.2 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −160.63 (q, J = 22.1 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.73 (d, J = 23.6 Hz), 148.53 (s), 147.37 (s), 128.00 (d, J = 3.4 Hz), 122.85 (s), 96.43 (d, J = 199.3 Hz), 75.79 (d, J = 22.9 Hz), 62.70 (s), 25.33 (d, J = 1.4 Hz), 19.42 (d, J = 23.2 Hz), 14.08 (s). IR (neat) ν = 2922, 2850, 1717, 1653, 1605, 1522, 1458, 1429, 1375, 1348, 1260, 1095, 855, 801, 728, 699 cm^{-1}. HRMS (ESI): calcd. for $[C_{13}H_{20}FN_2O_5]$ $(M+NH_4)^+$: 303.1351, found 303.1349.

Ethyl-2-fluoro-2-methyl-3-((4-methylphenyl)sulfonamido)-3-(4-(trifluoromethoxy)phenyl) propanoate (**3n**):74%, *syn*: *anti* = 45:55. ***syn*** – **3n:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 7.5 Hz, 2H), 7.08 (d, J = 8.6 Hz, 2H), 7.03 – 6.95 (m, 4H). 5.68 (d, J = 10.2 Hz, 1H), 4.82 (dd, J = 23.8, 10.1 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.30 (s, 3H), 1.37 (d, J = 23.1 Hz, 3H), 1.35(t, J = 7.1 Hz, 3H).^{19}F NMR (376 MHz, $CDCl_3$) δ −57.99 (s, 3F), −161.86 – −176.21 (m, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.95 (d, J = 25.6 Hz), 149.00 (s), 143.36 (s), 137.30 (s), 133.19 (s), 129.88 (d, J = 1.8 Hz), 129.13 (s), 126.85 (s), 120.66 (s), 120.37 (q, J = 256.6 Hz), 96.26 (d, J = 192.8 Hz), 62.59 (s), 61.76 (d, J = 20.5 Hz), 21.40 (d, J = 23.3 Hz), 21.19 (s), 14.06 (s). IR (neat) ν = 2923, 2852, 1735, 1458, 1376, 1259, 1221, 1116, 1073, 804, 668 cm^{-1}. HRMS (ESI): calcd. for $[C_{20}H_{22}F_4NO_5S]$ $(M+H)^+$: 464.1149, found 464.1150. ***anti*** – **3n:** H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 7.5 Hz, 2H), 6.99 (d, J = 8.1 Hz, 4H), 6.88 (d, J = 8.0 Hz, 2H), 5.47 (d, J = 9.9 Hz, 1H), 4.70 (dd, J = 25.5, 9.6 Hz, 1H), 4.01 – 3.86 (m, 2H), 2.31 (s, 3H), 1.76 (d, J = 23.5 Hz, 3H), 0.96 (t, J = 7.1 Hz, 3H).^{19}F NMR (376 MHz, $CDCl_3$) δ −58.05 (s, 3F), −169.10 – −169.39 (m, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.25 (d, J = 23.8 Hz), 148.91 (s), 143.58 (s), 137.02 (s), 134.09 (s), 129.63 (d, J = 2.2 Hz), 129.26 (s), 126.90 (s), 120.58 (s), 120.26 (q, J = 257.4 Hz), 96.97 (d, J = 195.0 Hz), 61.95 (s), 61.10 (d, J = 18.6 Hz), 21.47 (d, J = 23.8 Hz), 21.23 (s), 13.69 (s). IR (neat) ν = 3277, 2920, 2849, 1762, 1735, 1598, 1508, 1446, 1376, 1330, 1261, 1222, 1163, 1116, 1093, 1075, 1020, 906, 846, 813, 664, 565, 545 cm^{-1}.HRMS (ESI): calcd. for $[C_{20}H_{22}F_4NO_5S]$ $(M+H)^+$: 464.1149, found 464.1149.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jfluchem.2016.11.012.

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