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# Diastereoselective Addition of Metal α-Fluoroenolates of Carboxylate Esters to *N-tert*-Butylsulfinyl Imines: Synthesis of α-Fluoro-β-amino Acids

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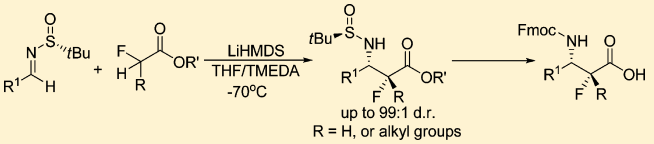
Supporting Information

**ABSTRACT:** We report a diastereoselective addition reaction of fluoroacetate and α-alkylated fluoroacetate to *N-tert*-butylsulfinyl imines. This method provides a concise route to α-fluoro-β-amino acids containing fluorinated quaternary stereogenic carbon centers with very good yields and high diastereoselectivities. This protocol has the benefit of using abundant and readily accessible starting materials and is operationally simple. Additionally, the stereochemical outcome of the present reaction was different from that of the previously known addition of comparable nonfluorinated, brominated, and chlorinated enolates to *N*-sulfinyl imines, suggesting that an open transition state (rather than a closed one) is involved in the current fluoroalkylation reaction.




## INTRODUCTION

Fluorine is known to affect the biological properties of organic compounds. The replacement of a C−H bond with a C−F bond can make the target molecule more bioavailable, lipophilic, and metabolically stable.[1] In this context, organic compounds with fluorine atom(s) bonded to $sp^3$-hybridized carbon atoms are of high importance[2] as they are present in many pharmaceuticals,[1,3] including the newly approved hepatitis C virus infection treatment drug sofosbuvir. Thus, there is great demand for the availability of versatile fluorinated building blocks featuring nonracemic stereogenic carbon−fluorine centers.[2,4]

Fluorinated β-amino acids are an important class of compounds as they have an integral role in bioactive molecules and peptidomimetics.[5] Proteins containing fluorinated β-amino acid residues have also been shown to have enhanced stability against chemical and thermal denaturation, and proteolytic degradation.[5a] In this context, the asymmetric synthesis of α-fluoro-β-amino acids has drawn a lot of attention.[6] For example, Seebach and co-workers described a multistep process starting from natural α-amino acids, involving deoxyfluorination of 3-amino-2-hydroxy carboxylic acid esters with DAST in the key step. However, a fluorination rearrangement occurs during the deoxyfluorination process, leading to a mixture of constitutional isomers.[6a] Electrophilic fluorination of chiral enolates has also been developed.[6b,c] However, the prerequisite chiral β-amino esters and the use of expensive fluorination reagents (such as NFSI) limit its practical use. Both strategies give 2,3-*anti* diastereoisomers as the major products. Recently, a base-promoted asymmetric Mannich reaction of fluorinated β-keto acetyloxazolidinone with *N*-acyloxyimines, followed by decarboxylation, was used to prepare α-fluoro β-amino acid derivatives.[7] However, significant racemization occurred during the decarboxylation process. For these reasons, a concise and efficient synthesis of α-fluoro-β-amino acids, particularly *syn*-configured α-fluoro-β-amino acids, is still highly desirable.

In the past decades, nucleophilic fluoroalkylation has been certified as a powerful strategy for the preparation of fluorinated compounds.[2,8] In this respect, α-fluoroenolates are important in synthetic organofluorine chemistry and have been widely used to prepare enantiopure α-fluorinated carbonyl compounds.[9,10] Particularly well developed is the use of α-fluoro-β-ketoesters as enolate precursors, and these have been deployed in a range of asymmetric reactions.[9] For simple ketones, aldehydes, and esters that are less acidic, their corresponding silyl α-fluoroenol ethers are frequently used.[10] However, using silyl α-fluoroenol ethers in typical addition reactions usually results in low stereoselectivities, and their preparation and purification is not trivial. Very recently, α-fluorinated β-keto *gem*-diols were developed to act as α-fluoroenolate equivalents in asymmetric condensation reactions, thus providing a novel method of constructing chiral $sp^3$ C−F centers.[11] The direct production of α-fluorinated carbonyl compounds from metal α-fluoroenolates generated *in situ* from simple fluoromethyl carbonyl compounds (such as fluoroacetate and fluoromethyl ketones) represents a highly attractive alternative, given the abundant and readily available precursors. However, the associated challenge of generating acyclic stereodefined enolates (of crucial importance to achieve high levels of stereocontrol)[12,13] and the relatively low stability of α-fluoro carbanions (due to the "negative fluorine effect")[8,14] were significant obstacles to their synthetic use. For a long time, only a few examples describing the addition of metal α-fluoroenolates (generated *in*

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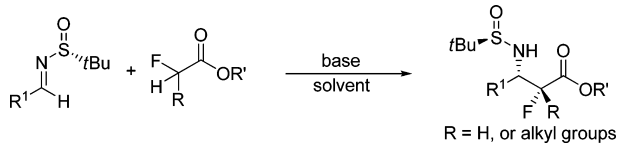
*situ* from fluoroacetate and fluoromethyl ketones) to aldehydes with only low to moderate stereoselectivities were known.[15] To the best of our knowledge, the general use of a metal $\alpha$-fluoroenolate of fluoroacetate in asymmetric synthesis has not yet been reported.[16] As part of our continued efforts in the synthesis of chiral halogenated amines,[17] we herein report the first general use of metal $\alpha$-fluoroenolates of carboxylate esters in asymmetric reactions. This enables the highly diastereoselective and concise synthesis of *syn*-configured $\alpha$-fluoro-$\beta$-amino acid derivatives from Ellman's *N*-*tert*-butanesulfinyl imines (Scheme 1).[18]

**Scheme 1. Synthesis of $\alpha$-Fluoro-$\beta$-amino Acids from $\alpha$-Fluorinated Carboxylate Esters**

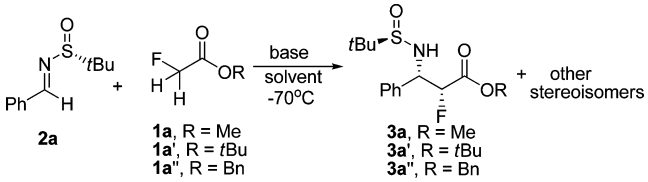



## RESULTS AND DISCUSSION

Methyl fluoroacetate **1a**, an abundant feedstock chemical, was first used as the fluorocarbon nucleophile, and its addition reaction with *N*-*tert*-butylsulfinyl imine **2a** was investigated. We initially followed a reported procedure for the addition of methyl fluoroacetate to aldehydes, and **2a** was added to the pregenerated enolate of **1a** (formed by deprotonation of **1a** with lithium hexamethyl disilazide (LiHMDS) in THF at −70 °C).[15a] However, the expected product was obtained in a very low yield with less than 10% of **1a** left intact (Table 1, entry 1), and this indicated that **1a** was readily decomposed under the reaction conditions. To our delight, when the *in situ* generated fluoroenolate was subjected to the reaction with **2a** (LiHMDS was added to a mixture of **1a** and **2a** in this case), the addition reaction proceeded smoothly, giving the product in 55% yield, with a diastereoselectivity of 80:13:7 (entry 2). Evaluation of other bases such as NaHMDS and KHMDS, and solvents including ether and toluene, demonstrated no improvements in yield and diastereoselectivity (entries 3−6). The inclusion of additives such as TMEDA and HMPA was also investigated (entries 7−12). While each was beneficial for promoting this transformation, TMEDA gave the best yield and diastereoselectivity (entry 8 vs entry 7). These observations indicated that the strong affinity of TMEDA for lithium ions plays an important role in achieving high levels of stereocontrol in the current fluoroalkylation reaction. Raising the temperature to −30 °C resulted in a decreased yield, but the diastereoselectivity remained high (entry 9). Under the optimal reaction conditions with the reactant ratios **2a**/**1a**/LiHMDS = 1:1.5:1.5 in the presence of TMEDA, product **3a** was afforded in 85% yield with a diastereoselectivity up to 95:3:2 (entry 10). The current reaction can be performed on a 10 mmol scale, furnishing the product in undiminished yield and diastereoselectivity. Easily accessible *t*-butyl fluoroacetate **3a′** and benzyl fluoroacetate **3a″** were also successfully subjected to the optimal reaction conditions (entry 11 and 12), affording the desired products with yields and diastereoselectivities comparable with those of methyl fluoroacetate.

Using fluoroacetate as the fluorocarbon nucleophile, we then evaluated the substrate scope of this reaction, and a wide array of structurally diverse imines (including nonenolizable,

**Table 1. Optimization of the Addition of Fluoroacetate to Ellman's Imine 2a**




**2a**

**1a**, R = Me
**1a′**, R = *t*Bu
**1a″**, R = Bn

**3a**, R = Me
**3a′**, R = *t*Bu
**3a″**, R = Bn

| entry | 1 | reactant ratio **2a**/**1a**/base | solvent/additive[a] | yield [%][b] | d.r.[c] |
|---|---|---|---|---|---|
| 1[d] | **1a** | 1:1.5:1.5 (LiHMDS) | THF | **3a**, <5 | n.d. |
| 2 | **1a** | 1:1.2:1.2 (LiHMDS) | THF | **3a**, 55 | 80:13:7 |
| 3 | **1a** | 1:1.2:1.2 (LiHMDS) | toluene | **3a**, 12 | 42:42:16 |
| 4 | **1a** | 1:1.2:1.2 (LiHMDS) | $Et_2O$ | **3a**, 15 | 47:40:13 |
| 5 | **1a** | 1:1.2:1.2 (KHMDS) | THF | **3a**, 30 | 87:9:4 |
| 6 | **1a** | 1:1.5:1.5 (NaHMDS) | THF | **3a**, 20 | 31:28:23:18 |
| 7 | **1a** | 1:1.2:1.2 (LiHMDS) | THF/HMPA | **3a**, 60 | 73:25:2 |
| 8 | **1a** | 1:1.2:1.2 (LiHMDS) | THF/TMEDA | **3a**, 65 | 92:6:2 |
| 9[e] | **1a** | 1:1.5:1.5 (LiHMDS) | THF/TMEDA | **3a**, 54[f] | 84:10:6 |
| 10 | **1a** | 1:1.5:1.5 (LiHMDS) | THF/TMEDA | **3a′**, 85[f] | 95:3:2 |
| 11 | **1a′** | 1:1.5:1.5 (LiHMDS) | THF/TMEDA | **3a′**, 84[f] | 90:9:1 |
| 12 | **1a″** | 1:1.5:1.5 (LiHMDS) | THF/TMEDA | **3a″**, 75[f] | 79:9:6:6 |

[a]A combination of 0.3 mL of additive (TMEDA or HMPA) and 3.0 mL of THF was used on a 1.0 mmol scale (for **2a**). [b]Yield was determined by $^{19}F$ NMR analysis with $PhCF_3$ as the internal standard. [c]d.r. was determined by $^{19}F$ NMR spectroscopy. [d]Reaction conditions: **2a** was added to the pregenerated enolate of **1a** in THF at −70 °C. [e]The reaction was carried out at −30 °C. [f]Isolated yield.

enolizable, aromatic, and heterocyclic imines) could be converted to the corresponding $\alpha$-fluoro-$\beta$-amino acid derivatives (Table 2). Substrates with electron-withdrawing or -donating substituents all performed well in this transformation (Table 2, entries 1−19). Notably, the reaction conditions tolerated a wide range of functional groups, including esters (**3g**), nitriles (**3i** and **3i′**), aryl halides (**3e**, **3e′**, **3e″**, and **3f**), and pyridines (**3l**). Even the strongly electronic-withdrawing nitro group tolerated the reaction conditions, delivering the products **3j** and **3j′** in moderate to good diastereoselectivities and high overall yield. The 2-naphthyl substrate underwent fluoroalkylation to give **3k** in 70% yield, with a diastereoselectivity up to a remarkable 99:0.5:0.5. Even aliphatic imines, which can be problematic substrates under strongly basic conditions, could be successfully transformed using the current conditions to give **3m** and **3n**. More importantly, ketimines also participated in the reaction, yielding the desired compounds containing an amino group attached to a tertiary carbon center (**3o** and **3p**). From these experimental findings, fluoroacetates **1a**, **1a′**, and **1a″** were all shown to work well in the fluoroalkylation reaction, and *t*-butyl fluoroacetate **1a′** gave better diastereoselectivities with electron-withdrawing substrates (**3i** vs **3i′** and **3j** vs **3j′**). The absolute configuration of **3e′** was determined by single-crystal X-ray analysis,[19] and the fluoro and amino substituents were found to adopt a *syn*


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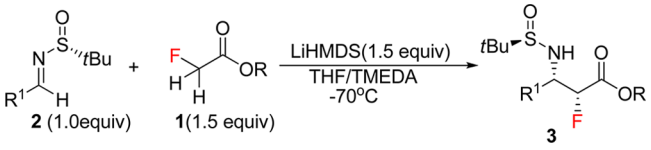
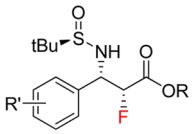
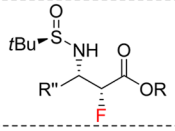
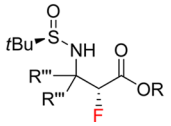
**Table 2. Survey of the Substrate Scope in the Fluoroalkylation of *N*-Sulfinylimines[a]**




| entry | products | | yield[%][b] | d.r.[c] |
|---|---|---|---|---|
| 1 |  | **3a**, R' = H, R = Me | 85 | 95:3:2 |
| 2 | | **3a'**, R' = H, R = *t*Bu | 85 | 90:9:1 |
| 3 | | **3a''**, R' = H, R = Bn | 75 | 79:9:6:6 |
| 4 | | **3b**, R' = 4-$CH_3$, R = Me | 80 | 92:6:2 |
| 5 | | **3b'**, R' = 4-$CH_3$, R = *t*Bu | 79 | 83:13:4 |
| 6 | | **3c**, R' = 3-$CH_3$, R = Me | 74 | 86:8:3:3 |
| 7 | | **3c'**, R' = 3-$CH_3$, R = *t*Bu | 81 | 86:9:5 |
| 8 | | **3d**, R' = 2-$CH_3$, R = Me | 76 | 84:7:6:3 |
| 9 | | **3e**, R' = 4-Cl, R = Me | 83 | 90:7:3 |
| 10 | | **3e'**, R' = 4- Cl, R = *t*Bu | 79 | 90:7:3 |
| 11 | | **3e''**, R' = 4- Cl, R = *Bn* | 78 | 86:11:3 |
| 12 | | **3f**, R' = 4- Br, R = *t*Bu | 76 | 92:4:3:1 |
| 13 | | **3g**, R' = 4-COOMe, R = Me | 65 | 86:14 |
| 14 | | **3h**, R' = 3-$CF_3$, R = Me | 77 | 85:15 |
| 15 | | **3h'**, R' = 3-$CF_3$, R = *t*Bu | 84 | 91:7:2 |
| 16 | | **3i**, R' = 4-CN, R = Me | 71 | 80:20 |
| 17 | | **3i'**, R' = 4-CN, R = *t*Bu | 75 | 86:9:3:2 |
| 18 | | **3j**, R' = 4-$NO_2$, R = Me | 57 | 79:21 |
| 19 | | **3j'**, R' = 4-$NO_2$, R = *t*Bu | 67 | 83:14:3 |
| 20 |  | **3k**, R''= 2-naphthyl, R = Me | 70 | 99:0.5:0.5 |
| 21 | | **3l**, R''= 2-pyridyl, R = Me | 70 | 84:16 |
| 22 | | **3m**, R''= *i*Pr, R = *t*Bu | 84 | 99:1 |
| 23 | | **3n**, R''= *t*Bu, R = *t*Bu | 82 | 85:14:1 |
| 24 |  | **3o**, R''' = $C_6H_5$, R = Me | 71 | 93:7 |
| 25 | | **3p**, R''' = 4-Cl$C_6H_4$, R = Me | 82 | 84:16 |

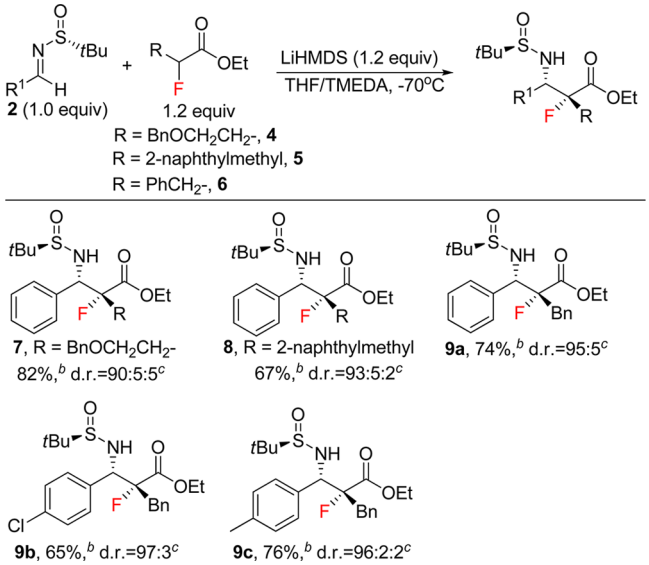
[a]Reaction conditions: LiHMDS (1.5 mL, 1.0 mol/L in THF) was added slowly to a reaction mixture of **1** (1.5 mmol), **2** (1.0 mmol) and TMEDA (0.3 mL) in THF (3.0 mL) at −70 °C. The reaction mixture was stirred for 0.5 h, followed by routine workup. [b]Isolated yields of the major stereoisomers. [c]d.r. was determined by $^{19}F$ NMR spectroscopy.

configuration. Note that either deoxyfluorination of the 3-amino-2-hydroxy carboxylic acid esters or fluorination of chiral enolates, led predominantly to *anti* diastereomers.[6] We anticipate that the current approach will be a valuable complement to existing synthetic methods.

The straightforward fluoroalkylation can be applied to α-alkylated fluoroacetate nucleophiles. As shown, fluorocarbon nucleophiles such as ethyl 4-(benzyloxy)-2-fluorobutanoate **4**, ethyl 2-fluoro-3-(naphthalen-2-yl)propanoate **5**, and ethyl 2-fluoro-3-phenylpropanoate **6** all reacted smoothly in the fluoroalkylation reactions, leading to α-fluoro β-amino acids **7**, **8**, and **9** containing quaternary stereogenic $sp^3$ C−F centers in a highly stereoselective manner (Scheme 2). The structure of **9c** was confirmed by X-ray crystallography.[19] Because quaternary carbon centers are known to provide conformational rigidity to fluorinated peptidomimetics,[5] the reported α-fluoro β-amino acids may find important applications in medicinal and life sciences.

To further demonstrate the usefulness of the reaction, compound **3a′** was converted to an Fmoc-protected derivative

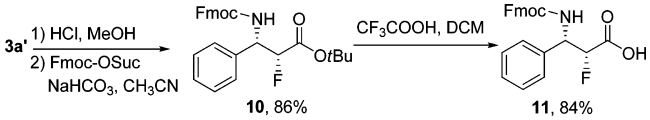
**Scheme 2. Synthesis of α-Fluoro-β-amino Acids Using α-Alkylated Fluoroacetates as Nucleophiles[a]**




[a]Reaction conditions: **2** (0.5 mmol), **4** (0.6 mmol), TMEDA (0.15 mL), LiHMDS (0.6 mmol), THF (1.5 mL), $N_2$, 0.5 h, −70 °C. [b]Isolated yields. [c]d.r. was determined by $^{19}F$ NMR spectroscopy.

suitable for use in solid-phase peptide synthesis. First, the removal of the *N*-*tert*-butylsulfinyl group using HCl/MeOH gave the corresponding ammonium salt, which was taken in crude form for Fmoc protection, affording **10** in 86% yield over the two steps. Deprotection of the *tert*-butyl ester in **10** with trifluoroacetic acid afforded enantiomerically pure **11** (Scheme 3).

**Scheme 3. Synthesis of the Fmoc-Protected α-Fluoro-β-amino Acid 11 from 3a′**




Welch and co-workers reported the addition of the metal α-fluoroenolate of ethyl fluoroacetate to aldehydes to give the expected aldol products with very low stereoselectivity (*syn*/*anti* = 1:1 to 1:3). This was attributed to the low selectivity in the Z/E enolate formation and difficulty in discriminating between the two prochiral faces of the enolate due to the similar size of fluorine and hydrogen.[15a] In sharp contrast, the present fluoroalkylation shows remarkably high diastereoselectivity for the addition reaction. On the basis of the variations in the diastereomeric ratios (Table 2), it is reasonable to assume that the addition reactions of E/Z fluoroenolates to *N*-sulfinyl imines undergo dynamic kinetic asymmetric transformations (or stereoconvergent processes),[20] leading to the formation of the major diastereomers with high levels of stereocontrol.

The observed diastereoselectivity can be tentatively explained based on an open transition state (Figure 1a). As shown, the sulfinyl oxygen of the imine is proposed to be in an *s-cis* arrangement with respect to the C=N bond,[17c,21] and the (*Z*)-enolate in an antiperiplanar orientation attacks the sterically less hindered Si face of the imine to afford the observed stereoselectivity. It should be pointed out that a comparable



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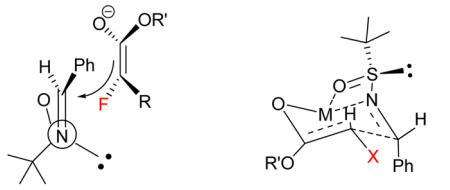


**Figure 1.** (a) Open transition-state mode proposed for the current fluoroalkylation reaction. (b) A closed transition-state mode reported for the addition of acetate, propionate, and bromoacetate to *N*-sulfinyl imines.

transition state mode was proposed for the addition of protected $\alpha$-hydroxyacetates to *N*-sulfinyl imines.[22] In contrast, the stereochemical outcome of the addition of metal enolates derived from methyl acetate and methyl propionate to *N*-*tert*-butylsulfinyl imines has been explained by a closed chairlike transition state (Figure 1b). The enolate attacks the Re face of (*R*)-*N*-*tert*-butylsulfinyl imines to give the products.[23] A similar transition state has been used to describe the observed stereoselectivities for the reaction of bromoacetate and dichloroacetate with *N*-sulfinyl imines (Figure 1b).[24,25] Evidently, introducing a single fluorine substituent imparts a significant effect on the characteristics of metal enolates, as the reactivity of the metal $\alpha$-fluoroenolates is different from their nonfluorinated, brominated, or chlorinated counterparts.

## CONCLUSIONS

We have successfully developed a concise, highly diastereoselective synthesis of $\alpha$-fluoro-$\beta$-amino acid derivatives, based on a straightforward addition of metal $\alpha$-fluoroenolates of carboxylate esters to *N*-*tert*-butylsulfinyl imines. The reaction uses abundant and readily available starting materials, has broad substrate scope, tolerates a variety of functional groups, and is operationally simple. Additionally, the stereochemical outcome of the reaction is different from that of the addition of comparable nonfluorinated, brominated, and chlorinated enolates to *N*-sulfinyl imines, demonstrating a marked fluorine effect. Further explorations of the applications of metal $\alpha$-fluoroenolates in asymmetic fluoroalkylation reactions are underway in our laboratory and will be reported in due course.

## EXPERIMENTAL SECTION

Unless otherwise mentioned, all commercial reagents and solvents were used directly as purchased without further purification. THF was distilled from sodium/benzophenone. TMEDA was treated with 4 Å molecular sieves before use. Melting points were uncorrected. Optical rotations were measured with a sodium lamp. NMR spectra were recorded on a spectrometer at 400 MHz ($^1$H NMR), 100 MHz ($^{13}$C NMR), and 376 MHz ($^{19}$F NMR). Chemical shifts ($\delta$) are reported in parts per million (ppm), and coupling constants ($J$) are given in Hertz (Hz). HRMS data using ESI were obtained on an ESI-FTMS mass spectrometer.

**Typical Procedure for the Diastereoselective Addition of Fluoroacetate 1 to *N*-*tert*-Butylsulfinyl Imine 2.** Under a $N_2$ atmosphere, LiHMDS (1.5 equiv, 1.5 mL, 1.0 mol/L in THF) was added slowly to a mixture of fluoroacetate **1** (1.5 mmol, 1.5 equiv), imine **2** (1.0 mmol, 1.0 equiv), TMEDA (0.3 mL), and THF (3 mL) at −70 °C. Reaction mixtures were stirred at this temperature for 30 min. Then, 1 N HCl (4 mL) was added, and the quenched reaction mixture was extracted three times with ethyl acetate (20 mL × 3). The combined organic layers were dried over anhydrous $MgSO_4$. Evaporation of the solvent under vacuum, followed by flash column chromatography on silica gel, gave the corresponding product **3**.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-phenyl-propionic Acid Methyl Ester (**3a**).* By following the general procedure, **3a** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (255 mg, 85%), mp 94−95 °C; $[\alpha]_D^{20}$ = +4.18 ($c$ = 0.52, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.46−7.33 (m, 5H), 5.18 (dd, $J$ = 47.2, 2.3 Hz, 1H), 4.98 (ddd, $J$ = 27.5, 9.3, 2.1 Hz, 1H), 4.06 (d, $J$ = 9.3 Hz, 1H), 3.83 (s, 3H), 1.22 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = −204.3 (dd, $J$ = 47.1, 26.9 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$): $\delta$ = 163.1 (d, $J$ = 24.7 Hz), 132.8, 124.1, 123.7, 122.4, 86.6 (d, $J$ = 192.6 Hz), 55.9 (d, $J$ = 18.9 Hz), 52.0, 47.8, 17.5. IR ($cm^{-1}$): 3292, 2957, 1750, 1454, 1438, 1226, 1075, 796. MS (ESI) $m/z$: 302.1 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{14}H_{21}FNO_3S^+$ $[M + H]^+$ 302.1221, found 302.1213.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-phenyl-propionic Acid tert-Butyl Ester (**3a′**).* By following the general procedure, **3a′** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1) as a white solid (291 mg, 85% yield), mp 107−108 °C; $[\alpha]_D^{20}$ = −16.49 ($c$ = 0.58, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.42 (d, $J$ = 7.2 Hz, 2H), 7.34 (dt, $J$ = 21.1, 7.1 Hz, 3H), 4.98 (dd, $J$ = 47.4, 2.8 Hz, 1H), 4.87 (ddd, $J$ = 10.7, 9.1, 2.5 Hz, 1H), 4.02 (d, $J$ = 8.7 Hz, 1H), 1.43 (s, 9H), 1.21 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −199.4 (dd, $J$ = 47.2, 24.8 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 166.3 (d, $J$ = 24.5 Hz), 137.8, 128.7, 128.4, 127.4, 91.2 (d, $J$ = 191.8 Hz), 83.5, 60.6 (d, $J$ = 19.3 Hz), 56.8, 27.9, 22.5. IR ($cm^{-1}$): 3298, 2968, 1721, 1474, 1458, 1322, 1158, 1071, 819. MS (ESI) $m/z$: 344.2 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{17}H_{27}FNO_3S^+$ $[M + H]^+$ 344.1690, found 344.1687.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-phenyl-propionic Acid Benzyl Ester (**3a″**).* By following the general procedure, **3a″** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1) as a yellow oil (283 mg, 75%); $[\alpha]_D^{20}$ = −3.63 ($c$ = 0.40, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.62−7.30 (m, 10H), 5.38−5.14 (m, 3H), 4.99 (ddd, $J$ = 26.5, 9.2, 2.5 Hz, 1H), 4.06 (d, $J$ = 9.2 Hz, 1H), 1.18 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −202.97 (dd, $J$ = 47.1, 26.4 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 162.4(d, $J$ = 24.8 Hz), 132.7, 129.7, 124.2, 124.1, 124.0, 123.9, 123.9, 123.8, 123.8, 123.7, 86.6 (d, $J$ = 192.7 Hz), 62.9, 55.9 (d, $J$ = 18.9 Hz), 52.0, 17.6. IR ($cm^{-1}$): 3329, 2960, 1760, 1497, 1455, 1364, 1263, 1202, 1063, 966, 746. MS (ESI) $m/z$: 378.2 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{20}H_{25}FNO_3S^+$ $[M + H]^+$ 378.1534, found 378.1536.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-p-tolyl-propionic Acid Methyl Ester (**3b**).* By following the general procedure, **3b** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (252 mg, 80%), mp 91−92 °C; $[\alpha]_D^{20}$ = +5.20 ($c$ = 0.50, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.33 (d, $J$ = 8.0 Hz, 2H), 7.21 (d, $J$ = 8.0 Hz, 2H), 5.15 (dd, $J$ = 47.2, 2.4 Hz, 1H), 4.93 (ddd, $J$ = 27.5, 9.3, 2.2 Hz, 1H), 4.00 (d, $J$ = 9.2 Hz, 1H), 3.82 (s, 3H), 2.36 (s, 3H), 1.21 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −204.2 (dd, $J$ = 46.9, 28.3 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 167.9 (d, $J$ = 24.8 Hz), 138.3, 134.5, 129.5, 127.1, 91.5 (d, $J$ = 192.3 Hz), 60.5 (d, $J$ = 18.9 Hz), 56.7, 52.5, 22.4, 21.0. IR ($cm^{-1}$): 3321, 2956, 1740, 1473, 1315, 1274, 1076, 880. MS (ESI) $m/z$: 338.1 $[M + Na]^+$. HRMS (ESI) $m/z$: calcd for $C_{15}H_{23}FNO_3S^+$ $[M + H]^+$ 316.1377, found 316.1371.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-p-tolyl- propionic acid tert-butyl ester (**3b′**).* By following the general procedure, **3b′** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1) as a white solid (282 mg, 79%), mp 112−113 °C; $[\alpha]_D^{20}$ = −19.85 ($c$ = 0.61, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.30 (d, $J$ = 7.8 Hz, 2H), 7.17 (d, $J$ = 7.8 Hz, 2H), 4.96 (dd, $J$ = 47.5, 2.8 Hz, 1H), 4.83 (ddd, $J$ = 25.1, 8.6, 2.3 Hz, 1H), 3.96 (d, $J$ = 8.6 Hz, 1H), 2.33 (s, 3H), 1.44 (s, 9H), 1.21 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −199.9 (dd, $J$ = 47.2, 25.0 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 166.3 (d, $J$ = 24.8 Hz), 138.2, 134.9, 129.4, 127.3, 91.3 (d, $J$ = 191.4 Hz), 83.4, 60.5 (d, $J$ = 19.1 Hz), 56.7, 28.0, 22.6, 21.1. IR ($cm^{-1}$): 3298, 2968, 1721, 1474, 1322, 1260, 1158,


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1071, 819. MS (ESI) $m/z$: 358.2 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{18}H_{29}FNO_3S^+$ $[M + H]^+$ 358.1847, found 358.1844.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-m-tolyl-propionic Acid Methyl Ester (**3c**).* By following the general procedure, **3c** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (233 mg, 74%), mp 89−90 °C; $[\alpha]_D^{20}$ = +0.23 ($c$ = 0.53, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.27 (dd, $J$ = 9.4, 6.1 Hz, 1H), 7.21 (d, $J$ = 6.3 Hz, 2H), 7.13 (d, $J$ = 7.2 Hz, 1H), 5.13 (dd, $J$ = 47.3, 1.8 Hz, 1H), 4.90 (dd, $J$ = 27.6, 9.3 Hz, 1H), 3.99 (d, $J$ = 9.1 Hz, 1H), 3.80 (s, 3H), 2.36 (s, 3H), 1.19 (s, 9H); $^{19}F$ NMR (376 MHz, $CDCl_3$) $\delta$ = −204.3 (dd, $J$ = 47.3, 27.4 Hz); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 167.9 (d, $J$ = 24.8 Hz), 138.5, 137.5, 129.2, 128.7, 127.9, 124.2, 91.4 (d, $J$ = 192.6 Hz), 60.7 (d, $J$ = 18.7 Hz), 56.7, 52.5, 22.4, 21.4. IR ($cm^{-1}$): 3295, 2851, 1750, 1456, 1355, 1297, 1072, 794. MS (ESI) $m/z$: 338.1 $[M + Na]^+$. HRMS (ESI) $m/z$: calcd for $C_{15}H_{22}FNO_3SNa^+$ $[M + Na]^+$ 338.1197, found 338.1194.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-m-tolyl-propionic Acid tert-Butyl Ester (**3c′**).* By following the general procedure, **3c′** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1) as a white solid (289 mg, 81%), mp 118−119 °C; $[\alpha]_D^{20}$ = −22.25 ($c$ = 0.53, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.30−7.19 (m, 3H), 7.12 (d, $J$ = 7.1 Hz, 1H), 4.96 (dd, $J$ = 47.5, 3.1 Hz, 1H), 4.81 (ddd, $J$ = 24.5, 8.5, 2.8 Hz, 1H), 3.97 (d, $J$ = 8.5 Hz, 1H), 2.35 (s, 3H), 1.43 (s, 9H), 1.21 (s, 9H); $^{19}F$ NMR (376 MHz, $CDCl_3$) $\delta$ = −199.2 (dd, $J$ = 47.3, 24.7 Hz); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 166.3 (d, $J$ = 24.5 Hz), 138.4, 136.6, 129.2, 128.6, 128.1, 124.5, 91.2 (d, $J$ = 191.6 Hz), 83.4, 60.7 (d, $J$ = 19.2 Hz), 56.7, 27.9, 22.5, 21.4. IR ($cm^{-1}$): 3285, 2978, 1742, 1473, 1368, 1055, 843, 796. MS (ESI) $m/z$: 358.2 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{18}H_{29}FNO_3S^+$ $[M + H]^+$ 358.1847, found 358.1843.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-o-tolyl-propionic Acid Methyl Ester (**3d**).* By following the general procedure, **3d** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (239 mg, 76%), mp 65−66 °C; $[\alpha]_D^{20}$ = +3.46 ($c$ = 0.52, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.26 (dd, $J$ = 9.1, 6.6 Hz, 1H), 7.21 (d, $J$ = 6.6 Hz, 2H), 7.13 (d, $J$ = 7.3 Hz, 1H), 5.13 (dd, $J$ = 47.2, 2.1 Hz, 1H), 4.90 (dd, $J$ = 27.6, 9.1 Hz, 1H), 3.98 (d, $J$ = 9.3 Hz, 1H), 3.80 (s, 3H), 2.36 (s, 3H), 1.19 (s, 9H); $^{19}F$ NMR (376 MHz, $CDCl_3$) $\delta$ = −204.3 (dd, $J$ = 46.9, 28.5 Hz); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 167.9 (d, $J$ = 24.7 Hz), 138.5, 137.5, 129.2, 128.7, 127.9, 124.2, 91.4 (d, $J$ = 192.6 Hz), 60.7 (d, $J$ = 18.7 Hz), 56.7, 52.5, 22.4, 21.4. IR ($cm^{-1}$): 3296, 2926, 1613, 1441, 1355, 1226, 1095, 794, 721. MS (ESI) $m/z$: 338.1 $[M + Na]^+$. HRMS (ESI) $m/z$: calcd for $C_{15}H_{22}FNO_3SNa^+$ $[M + Na]^+$ 338.1197, found 338.1194.

*($R_S$,2S,3R)-3-(4-Chloro-phenyl)-2-fluoro-3-(2-methylpropane-2-sulfinylamino)-propionic Acid Methyl Ester (**3e**).* By following the general procedure, **3e** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (279 mg, 83%), mp 77−78 °C; $[\alpha]_D^{20}$ = −14.8 ($c$ = 0.55, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.60−7.32 (m, 4H), 5.15 (dd, $J$ = 47.2, 2.3 Hz, 1H), 4.95 (ddd, $J$ = 27.4, 9.7, 2.2 Hz, 1H), 4.06 (d, $J$ = 9.7 Hz, 1H), 3.84 (s, 3H), 1.21 (s, 9H) ; $^{19}F$ NMR (376 MHz, $CDCl_3$) $\delta$ = −204.3 (dd, $J$ = 46.9, 28.2 Hz); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 167.6 (d, $J$ = 24.3 Hz), 136.0, 134.5, 129.0, 128.6, 91.1 (d, $J$ = 192.9 Hz), 60.0 (d, $J$ = 19.0 Hz), 56.8, 52.6, 22.3. IR ($cm^{-1}$): 3325, 2960, 1771, 1496, 1456, 1276, 1018, 837, 811. MS (ESI) $m/z$: 358.1 $[M + Na]^+$. HRMS (ESI) $m/z$: calcd for $C_{14}H_{20}ClFNO_3S^+$ $[M + H]^+$ 336.0831, found 336.0840.

*($R_S$,2S,3R)-3-(4-Chloro-phenyl)-2-fluoro-3-(2-methylpropane-2-sulfinylamino)-propionic Acid tert-Butyl Ester (**3e′**).* By following the general procedure, **3e′** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1) as a white solid (299 mg, 79%), mp 123−124 °C; $[\alpha]_D^{20}$ = +29.10 ($c$ = 0.53, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.36 (q, $J$ = 8.7 Hz, 4H), 4.95 (dd, $J$ = 47.4, 2.2 Hz, 1H), 4.87−4.78 (m, 1H), 4.05 (d, $J$ = 9.3 Hz, 1H), 1.45 (s, 9H), 1.21 (s, 9H); $^{19}F$ NMR (376 MHz, $CDCl_3$) $\delta$ = −199.6 (dd, $J$ = 48.6, 25.8 Hz); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 166.0 (d, $J$ = 24.2 Hz), 136.4, 134.4, 128.9, 90.9 (d, $J$ = 192.6 Hz), 83.7, 59.9 (d, $J$ = 19.5 Hz), 56.9, 28.0, 22.5. IR ($cm^{-1}$): 3309, 2964, 1720, 1496, 1474, 1319, 1261, 1070, 882. MS (ESI) $m/z$: 379.0 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{17}H_{25}ClFNO_3SNa^+$ $[M + Na]^+$ 400.1120, found 400.1139.

*($R_S$,2S,3R)-3-(4-Chloro-phenyl)-2-fluoro-3-(2-methylpropane-2-sulfinylamino)-propionic Acid Benzyl Ester (**3e″**).* By following the general procedure, **3e″** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1) as a white solid (321 mg, 78%), mp 102−103 °C; $[\alpha]_D^{20}$ = +7.01 ($c$ = 0.50, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.41−7.35 (m, 9H), 5.23 (dd, $J$ = 29.7, 12.0 Hz, 2H), 5.16 (dd, $J$ = 47.1, 2.5 Hz, 1H), 4.95 (ddd, $J$ = 26.0, 9.5, 2.4 Hz, 1H), 4.06 (d, $J$ = 9.5 Hz, 1H), 1.17 (s, 9H); $^{19}F$ NMR (376 MHz, $CDCl_3$) $\delta$ = −202.60 (dd, $J$ = 48.7, 27.3 Hz); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 167.0 (d, $J$ = 24.7 Hz), 140.8, 135.9, 134.5, 134.3, 129.0, 128.8, 128.7, 128.7, 128.5, 127.6, 126.9, 91.1 (d, $J$ = 193.3 Hz), 67.7, 65.3, 60.1 (d, $J$ = 19.2 Hz), 56.8, 22.3. IR ($cm^{-1}$): 3329, 3029, 1739, 1494, 1455, 1358, 1172, 1089, 885. MS (ESI) $m/z$: 434.1 $[M + Na]^+$. HRMS (ESI) $m/z$: calcd for $C_{20}H_{23}ClFNO_3SNa^+$ $[M + Na]^+$ 434.0963, found 434.0977.

*($R_S$,2S,3R)-3-(4-Bromo-phenyl)-2-fluoro-3-(2-methylpropane-2-sulfinylamino)-propionic Acid tert-Butyl Ester (**3f**).* By following the general procedure, **3f** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1) as a white solid (321 mg, 76%), mp 124−125 °C; $[\alpha]_D^{20}$ = −5.60 ($c$ = 0.58, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.50 (d, $J$ = 8.4 Hz, 2H), 7.31 (d, $J$ = 8.2 Hz, 2H), 4.95 (dd, $J$ = 47.3, 2.5 Hz, 1H), 4.83 (ddd, $J$ = 25.0, 9.4, 2.2 Hz, 1H), 4.05 (d, $J$ = 9.4 Hz, 1H), 1.45 (s, 9H), 1.20 (s, 9H); $^{19}F$ NMR (376 MHz, $CDCl_3$) $\delta$ = −199.9 (dd, $J$ = 47.1, 24.8 Hz); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 166.0 (d, $J$ = 24.2 Hz), 136.9, 131.8, 129.2, 122.6, 90.8 (d, $J$ = 192.5 Hz), 83.8, 60.0 (d, $J$ = 19.4 Hz), 56.9, 28.0, 22.5. IR ($cm^{-1}$): 3308, 2987, 1719, 1491, 1362, 1296, 1070, 832. MS (ESI) $m/z$: 422.1 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{17}H_{26}BrFNO_3S^+$ $[M + H]^+$ 422.0795, found 422.0793.

*($R_S$,2S,3R)-4-[2-Fluoro-2-methoxycarbonyl-1-(2-methylpropane-2-sulfinylamino)-ethyl]-benzoic Acid Methyl Ester (**3g**).* By following the general procedure, **3g** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (233 mg, 65%), mp 62−63 °C; $[\alpha]_D^{20}$ = +12.2 ($c$ = 0.42, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 8.06 (d, $J$ = 8.3 Hz, 2H), 7.51 (d, $J$ = 8.1 Hz, 2H), 5.16 (dd, $J$ = 47.2, 1.9 Hz, 1H), 5.01 (dd, $J$ = 27.3, 10.0 Hz, 1H), 4.14 (d, $J$ = 9.6 Hz, 1H), 3.91 (s, 3H), 3.82 (s, 3H), 1.19 (s, 9H); $^{19}F$ NMR (376 MHz, $CDCl_3$) $\delta$ = −204.2 (dd, $J$ = 47.0, 28.0 Hz); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 167.5 (d, $J$ = 24.6 Hz), 166.5, 142.4, 130.3, 130.1, 127.3, 91.1 (d, $J$ = 193.4 Hz), 60.2 (d, $J$ = 19.0 Hz), 56.9, 52.7, 52.2, 22.4. IR ($cm^{-1}$): 3426, 2921, 1769, 1436, 1366, 1277, 1042, 927. MS (ESI) $m/z$: 382.1 $[M + Na]^+$. HRMS (ESI) $m/z$: calcd for $C_{16}H_{22}FNO_5SNa^+$ $[M + Na]^+$ 382.1095, found 382.1087.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-(3-trifluoromethyl-phenyl)-propionic Acid Methyl Ester (**3h**).* By following the general procedure, **3h** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (284 mg, 77%), mp 63−65 °C; $[\alpha]_D^{20}$ = +7.64 ($c$ = 0.50, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.65 (d, $J$ = 9.1 Hz, 2H), 7.60 (d, $J$ = 7.5 Hz, 1H), 7.52 (t, $J$ = 7.5 Hz, 1H), 5.16 (dd, $J$ = 47.1, 1.2 Hz, 1H), 5.01 (dd, $J$ = 27.4, 9.7 Hz, 1H), 4.13 (d, $J$ = 9.8 Hz, 1H), 3.82 (s, 3H), 1.18 (s, 9H); $^{19}F$ NMR (376 MHz, $CDCl_3$) $\delta$ = −62.6 (s, 3F), −204.5 (dd, $J$ = 47.1, 26.9 Hz, 1F); $^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta$ = 167.4 (d, $J$ = 24.4 Hz), 138.6, 130.9, 129.4, 125.4 (d, $J$ = 3.7 Hz), 124.0 (d, $J$ = 3.5 Hz), 91.0 (d, $J$ = 193.3 Hz), 60.2 (d, $J$ = 18.9 Hz), 57.0, 52.7, 29.6, 22.3. IR ($cm^{-1}$): 3315, 2917, 1748, 1440, 1323, 1086, 1076, 819. MS (ESI) $m/z$: 392.1 $[M + Na]^+$. HRMS (ESI) $m/z$: calcd for $C_{15}H_{19}F_4NO_3SNa^+$ $[M + Na]^+$ 392.0914, found 392.0904.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-(3-trifluoromethyl-phenyl)-propionic Acid tert-Butyl Ester (**3h′**).* By following the general procedure, **3h′** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (345 mg, 84%), mp 99−100 °C; $[\alpha]_D^{20}$ = −2.57 ($c$ = 0.52, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ = 7.66 (d, $J$ = 7.5 Hz, 2H), 7.60 (d, $J$ = 7.5 Hz, 1H), 7.51 (t, $J$ = 7.6 Hz, 1H), 4.99 (dd, $J$ = 47.1, 2.7 Hz, 1H), 4.94 (ddd, $J$ = 24.3, 9.4, 2.5 Hz, 1H), 4.16 (d, $J$ = 9.3



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Hz, 1H), 1.44 (s, 9H), 1.22 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −62.6 (s, 3F), −199.1 (dd, $J$ = 48.8, 25.5 Hz, 1F); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 165.9 (d, $J$ = 24.2 Hz), 138.8, 131.1, 129.3, 125.3 (d, $J$ = 3.5 Hz), 124.2 (d, $J$ = 2.6 Hz), 90.7 (d, $J$ = 193.1 Hz), 83.9, 77.2, 60.0 (d, $J$ = 19.6 Hz), 57.0, 27.9, 22.5. IR (cm$^{-1}$): 3323, 2975, 1744, 1473, 1333, 1171, 1129, 1043, 873. MS (ESI) $m/z$: 412.2 [M + H]$^+$. HRMS (ESI) $m/z$: calcd for $C_{18}H_{26}F_4NO_3S^+$ [M + H]$^+$ 412.1564, found 412.1559.

*($R_S$,2S,3R)-3-(4-Cyano-phenyl)-2-fluoro-3-(2-methylpropane-2-sulfinylamino)-propionic Acid Methyl Ester (**3i**).* By following the general procedure, **3i** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (231 mg, 71%), mp 113−114 °C; $[\alpha]_D^{20}$ = +29.1 ($c$ = 0.53, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.68 (d, $J$ = 8.3 Hz, 2H), 7.56 (d, $J$ = 8.2 Hz, 2H), 5.15 (dd, $J$ = 47.1, 1.9 Hz, 1H), 4.99 (dd, $J$ = 27.3, 10.2 Hz, 1H), 4.16 (d, $J$ = 10.2 Hz, 1H), 3.82 (s, 3H), 1.18 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −204.3 (dd, $J$ = 47.0, 27.8 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 167.2 (d, $J$ = 24.5 Hz), 142.7, 132.6, 128.1, 118.2, 112.5, 90.8 (d, $J$ = 193.8 Hz), 60.4 (d, $J$ = 19.1 Hz), 57.0, 52.8, 22.3. IR (cm$^{-1}$): 3307, 2961, 2226, 1735, 1444, 1360, 1291, 1061, 850. MS (ESI) $m/z$: 327.1 [M + H]$^+$. HRMS (ESI) $m/z$: calcd for $C_{15}H_{19}FN_2O_3SNa^+$ [M + Na]$^+$ 349.0993, found 349.0986.

*($R_S$,2S,3R)-3-(4-Cyano-phenyl)-2-fluoro-3-(2-methylpropane-2-sulfinylamino)-propionic Acid tert-Butyl Ester (**3i′**).* By following the general procedure, **3i′** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (276 mg, 75%), mp 121−122 °C; $[\alpha]_D^{20}$ = +1.75 ($c$ = 0.55, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.67 (d, $J$ = 8.3 Hz, 2H), 7.57 (d, $J$ = 8.2 Hz, 2H), 4.98 (dd, $J$ = 47.0, 2.3 Hz, 1H), 4.93 (ddd, $J$ = 15.8, 11.8, 2.2 Hz, 1H), 4.20 (d, $J$ = 9.8 Hz, 1H), 1.46 (s, 9H), 1.21 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −199.5 (dd, $J$ = 46.5, 23.4 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 165.7 (d, $J$ = 23.9 Hz), 143.1, 132.4, 128.3, 118.3, 112.4, 90.4 (d, $J$ = 193.9 Hz), 84.1, 60.2 (d, $J$ = 19.6 Hz), 57.1, 28.0, 22.5. IR (cm$^{-1}$): 3334, 2978, 2231, 1750, 1473, 1355, 1252, 1156, 881. MS (ESI) $m/z$: 369.2 [M + H]$^+$. HRMS (ESI) $m/z$: calcd for $C_{18}H_{26}FN_2O_3S^+$ [M + H]$^+$ 369.1643, found 369.1636.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-(4-nitro-phenyl)-propionic Acid Methyl Ester (**3j**).* By following the general procedure, **3j** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (197 mg, 57%), mp 80−81 °C; $[\alpha]_D^{20}$ = +28.0 ($c$ = 0.53, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 8.25 (d, $J$ = 8.8 Hz, 2H), 7.63 (d, $J$ = 8.7 Hz, 2H), 5.17 (dd, $J$ = 47.2, 2.0 Hz, 1H), 5.05 (dd, $J$ = 27.4, 10.4 Hz, 1H), 4.21 (d, $J$ = 10.2 Hz, 1H), 3.83 (s, 3H), 1.19 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −204.2 (dd, $J$ = 46.9, 28.1 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 167.2 (d, $J$ = 24.4 Hz), 147.9, 144.5, 128.4, 124.0, 90.82 (d, $J$ = 193.9 Hz), 60.1 (d, $J$ = 19.1 Hz), 57.1, 52.8, 22.3. IR (cm$^{-1}$): 3119, 2965, 1737, 1525, 1439, 1348, 1275, 1008, 932. MS (ESI) $m/z$: 368.9 [M + Na]$^+$. HRMS (ESI) $m/z$: calcd for $C_{14}H_{19}FN_2O_5SNa^+$ [M + Na]$^+$ 369.0891, found 369.0900.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-(4-nitro-phenyl)-propionic Acid tert-Butyl Ester (**3j′**).* By following the general procedure, **3j′** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (260 mg, 67%), mp 99−100 °C; $[\alpha]_D^{20}$ = +7.90 ($c$ = 0.57, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 8.23 (d, $J$ = 8.7 Hz, 2H), 7.63 (d, $J$ = 8.6 Hz, 2H), 5.10−4.86 (m, 2H), 4.25 (d, $J$ = 9.9 Hz, 1H), 1.47 (s, 9H), 1.22 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −199.8 (dd, $J$ = 47.2, 24.3 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 165.7 (d, $J$ = 23.9 Hz), 147.8, 145.0, 128.6, 123.8, 90.4 (d, $J$ = 194.1 Hz), 84.2, 59.9 (d, $J$ = 19.6 Hz), 57.1, 28.0, 22.5. IR (cm$^{-1}$): 3342, 2981, 1752, 1473, 1357, 1253, 1156, 848, 765. MS (ESI) $m/z$: 389.2 [M + H]$^+$. HRMS (ESI) $m/z$: calcd for $C_{17}H_{26}FN_2O_5S^+$ [M + H]$^+$ 389.1541, found 389.1533.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-naphthalen-2-yl-propionic Acid Methyl Ester (**3k**).* By following the general procedure, **3k** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (246 mg, 70%), mp 111−113 °C; $[\alpha]_D^{20}$ = +16.17 ($c$ = 0.51, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.95−7.78 (m, 4H), 7.61−7.44 (m, 3H), 5.25 (d, $J$ = 47.2 Hz, 1H), 5.12 (dd, $J$ = 27.5, 9.2 Hz, 1H), 4.16 (d, $J$ = 9.3 Hz, 1H), 3.82 (s, 3H), 1.20 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −204.0 (dd, $J$ = 47.0, 28.2 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 167.8 (d, $J$ = 24.8 Hz), 134.9, 133.1, 128.8, 128.2, 127.6, 126.6, 126.5, 126.4, 124.7, 91.4 (d, $J$ = 192.7 Hz), 60.7 (d, $J$ = 18.8 Hz), 56.8, 52.6, 22.4. IR (cm$^{-1}$): 3296, 2958, 1439, 1353, 1285, 1073, 931, 875, 800. MS (ESI) $m/z$: 374.1 [M + Na]$^+$. HRMS (ESI) $m/z$: calcd for $C_{18}H_{22}FNO_3SNa^+$ [M + Na]$^+$ 374.1197, found 374.1189.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-3-pyridin-2-yl-propionic Acid Methyl Ester (**3l**).* By following the general procedure, **3l** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/2) as a white solid (212 mg, 70%), mp 110−111 °C; $[\alpha]_D^{20}$ = +4.77 ($c$ = 0.57, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 8.58 (d, $J$ = 4.7 Hz, 1H), 7.72 (t, $J$ = 7.7 Hz, 1H), 7.54 (d, $J$ = 7.8 Hz, 1H), 7.20−7.24 (m, 1H), 5.47 (dd, $J$ = 46.9, 2.4 Hz, 1H), 5.07 (dd, $J$ = 26.2, 9.2 Hz, 1H), 4.89 (d, $J$ = 9.1 Hz, 1H), 3.80 (s, 3H), 1.26 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −204.5 (dd, $J$ = 46.8, 26.1 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 167.9 (d, $J$ = 24.5 Hz), 155.8, 149.0, 137.0, 123.1, 122.0, 91.0 (d, $J$ = 191.4 Hz), 62.0 (d, $J$ = 19.8 Hz), 56.7, 52.4, 22.5. IR (cm$^{-1}$): 3251, 2959, 1760, 1592, 1438, 1347, 1234, 1075, 993. MS (ESI) $m/z$: 303.1 [M + H]$^+$. HRMS (ESI) $m/z$: calcd for $C_{13}H_{20}FN_2O_3S^+$ [M + H]$^+$ 303.1173, found 303.1170.

*($R_S$,2S,3R)-2-Fluoro-4-methyl-3-(2-methylpropane-2-sulfinylamino)-pentanoic Acid tert-Butyl Ester (**3m**).* By following the general procedure, **3m** was isolated by column chromatography on silica gel (dichloromethane/methanol = 100/1) as a white solid (260 mg, 84%), mp 82−83 °C; $[\alpha]_D^{20}$ = −32.70 ($c$ = 0.53, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 4.88 (d, $J$ = 47.9 Hz, 1H), 3.53 (qd, $J$ = 15.4, 9.2 Hz, 2H), 2.07 (dd, $J$ = 12.9, 6.7 Hz, 1H), 1.48 (s, 9H), 1.21 (s, 9H), 1.06 (dd, $J$ = 12.1, 4.4 Hz, 6H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −203.1 (dd, $J$ = 47.9, 31.0 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 167.2 (d, $J$ = 25.1 Hz), 88.7 (d, $J$ = 188.1 Hz), 83.1, 62.9 (d, $J$ = 17.9 Hz), 56.7, 32.0, 28.1, 22.7, 19.5, 18.7. IR (cm$^{-1}$): 3256, 2978, 1756, 1559, 1469, 1360, 1280, 1148, 860. MS (ESI) $m/z$: 310.2 [M + H]$^+$. HRMS (ESI) $m/z$: calcd for $C_{14}H_{29}FNO_3S^+$ [M + H]$^+$ 310.1847, found 310.1845.

*($R_S$,2S,3R)-2-Fluoro-4,4-dimethyl-3-(2-methylpropane-2-sulfinylamino)-pentanoic Acid tert-Butyl Ester (**3n**).* By following the general procedure, **3n** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (265 mg, 82%), mp 111.2−111.5 °C; $[\alpha]_D^{20}$ = −42.38 ($c$ = 0.62, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 4.99 (d, $J$ = 47.9 Hz, 1H), 3.61 (d, $J$ = 9.3 Hz, 1H), 3.46 (dd, $J$ = 28.3, 9.2 Hz, 1H), 1.49 (s, 9H), 1.22 (s, 9H), 1.08 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −202.7 (dd, $J$ = 47.8, 28.6 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 162.7 (d, $J$ = 25.1 Hz), 83.3 (d, $J$ = 188.1 Hz), 78.3, 60.9 (d, $J$ = 17.0 Hz), 52.2, 29.8, 23.4, 23.2, 22.6, 18.1. IR (cm$^{-1}$): 3254, 2958, 1762, 1475, 1368, 1234, 1159, 1062, 998. MS (ESI) $m/z$: 324.2 [M + H]$^+$. HRMS (ESI) $m/z$: calcd for $C_{15}H_{31}FNO_3S^+$ [M + H]$^+$ 324.2003, found 324.2002.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-4,4-diphenyl- butyric Acid Methyl Ester (**3o**).* By following the general procedure, **3o** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (267 mg, 71%), mp 112−113 °C; $[\alpha]_D^{20}$ = −23.01 ($c$ = 0.57, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.63 (d, $J$ = 7.8 Hz, 2H), 7.29−7.42 (m, 6H), 7.12−7.28 (m, 2H), 5.72 (d, $J$ = 47.5 Hz, 1H), 5.50 (s, 1H), 3.46 (s, 3H), 1.23 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −185.73 (d, $J$ = 47.2 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 169.0 (d, $J$ = 23.2 Hz), 139.3, 138.3, 129.3, 128.8, 128.7, 128.4, 128.2, 128.0, 92.3 (d, $J$ = 206.8 Hz), 69.2 (d, $J$ = 20.8 Hz), 56.5, 52.5, 22.9. IR (cm$^{-1}$): 3316, 2853, 1446, 1301, 1172, 1069, 867, 821. MS (ESI) $m/z$: 400.1 [M + Na]$^+$. HRMS (ESI) $m/z$: calcd for $C_{20}H_{24}FNO_3SNa^+$ [M + Na]$^+$ 400.1353, found 400.1365.

*($R_S$,2S,3R)-3,3-Bis(4-chloro-phenyl)-2-fluoro-3-(2-methylpropane-2-sulfinylamino)-propionic Acid Methyl Ester (**3p**).* By following the general procedure, **3p** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1) as a white solid (366 mg, 82%), mp 101−102 °C; $[\alpha]_D^{20}$ = −3.98 ($c$ = 0.58, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.58 (d, $J$ = 7.6 Hz, 2H), 7.33 (dd, $J$ = 8.7, 4.9 Hz, 4H), 7.13 (d, $J$ = 8.5 Hz, 2H), 5.63 (d, $J$ = 47.5 Hz, 1H), 5.52 (s, 1H), 3.53 (s, 3H), 1.22 (s, 9H); $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ = −186.0 (d, $J$ = 47.1 Hz); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ = 168.8



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(d, $J$ = 22.8 Hz), 137.5, 136.2, 134.8, 134.5, 131.1, 130.7, 130.2, 130.1, 128.6, 128.3, 92.0 (d, $J$ = 208.2 Hz), 68.7 (d, $J$ = 20.9 Hz), 56.7, 52.8, 22.9. IR ($cm^{-1}$): 3319, 2956, 1770, 1493, 1402, 1300, 1281, 1095, 873. MS (ESI) $m/z$: 445.9 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{20}H_{22}Cl_2FNO_3SNa^+$ $[M + Na]^+$ 468.0574, found 468.0551.

**Typical Procedure for the Diastereoselective Addition of α-Alkylated Fluoroacetate to *N*-*tert*-Butylsulfinyl Imines.** Under $N_2$ atmosphere, LiHMDS (0.6 mL, 1.0 mol/L in THF, 1.2 equiv) was added slowly to a mixture of α-alkylated fluoroacetate (0.6 mmol, 1.2 equiv), imine **2** (0.5 mmol, 1.0 equiv), TMEDA (0.15 mL), and THF (1.5 mL) at −70 °C. Reaction mixtures were stirred at this temperature for 30 min. Then, 1 N HCl (2 mL) was added, and the quenched reaction mixture was extracted three times with ethyl acetate (10 mL × 3). The combined organic layers were dried over anhydrous $MgSO_4$. Evaporation of the solvent under vacuum, followed by flash column chromatography on silica gel, gave the corresponding product **7**, **8**, or **9**.

*($R_S$,2S,3R)-4-Benzyloxy-2-fluoro-2-[(2-methylpropane-2-sulfinylamino)-phenyl-methyl]-butyric Acid Ethyl Ester (**7**).* By following the general procedure, **7** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (184 mg, 82%), mp 123.5−124.2 °C; $[\alpha]_D^{20}$ = −8.85 ($c$ = 0.57, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ = 7.26−7.39 (m, 10H), 4.61 (dd, $J$ = 26.3, 10.6 Hz, 1H), 4.37 (s, 2H), 3.99−4.11 (m, 3H), 3.47 (dddd, $J$ = 18.6, 13.9, 9.4, 4.5 Hz, 2H), 2.08−2.32 (m, 2H), 1.19 (t, $J$ = 7.2 Hz, 3H), 1.15 (s, 9H); $^{19}F$ NMR (376 MHz, $CDCl_3$) δ = −180.9 (t, $J$ = 30.7 Hz); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ = 169.7 (d, $J$ = 26.3 Hz), 137.7, 136.9, 128.7, 128.6, 128.5, 128.2, 127.8, 127.6, 97.5 (d, $J$ = 195.1 Hz), 73.2, 65.5 (d, $J$ = 18.7 Hz), 64.1 (d, $J$ = 4.0 Hz), 61.7, 56.5, 35.3 (d, $J$ = 21.4 Hz), 22.3, 13.9. IR ($cm^{-1}$): 3321, 2962, 1730, 1470, 1322, 1221, 1151, 1098, 1030, 879. MS (ESI) $m/z$: 450.2 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{24}H_{33}FNO_4S^+$ $[M + H]^+$ 450.2109, found 450.2100.

*($R_S$,2S,3R)-2-Fluoro-3-(2-methylpropane-2-sulfinylamino)-2-naphthalen-2-ylmethyl-3-phenyl-propionic Acid Ethyl Ester (**8**).* By following the general procedure, **8** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (153 mg, 67%), mp 147.9−148.7 °C; $[\alpha]_D^{20}$ = +7.11 ($c$ = 0.52, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ = 7.63−7.87 (m, 3H), 7.55 (s, 1H), 7.32−7.51 (m, 7H), 7.22 (d, $J$ = 8.4 Hz, 1H), 4.81 (dd, $J$ = 25.7, 10.5 Hz, 1H), 4.10 (d, $J$ = 10.7 Hz, 1H), 3.99 (q, $J$ = 7.1 Hz, 2H), 3.14 (dd, $J$ = 39.3, 14.5 Hz, 1H), 2.82 (t, $J$ = 13.7 Hz, 1H), 1.16 (s, 9H), 0.98 (t, $J$ = 7.1 Hz, 3H); $^{19}F$ NMR (376 MHz, $CDCl_3$) δ = −177.4 (br); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ = 169.2 (d, $J$ = 25.6 Hz), 136.9, 133.1, 132.5, 131.2, 128.9, 128.8, 128.8, 128.5, 127.9, 127.8, 127.5, 127.5, 125.9, 125.7, 100.1 (d, $J$ = 198.9 Hz), 65.6 (d, $J$ = 18.7 Hz), 61.7, 56.6, 41.6 (d, $J$ = 20.9 Hz), 22.3, 13.9. IR ($cm^{-1}$): 3319, 2959, 1716, 1508, 1457, 1328, 1223, 1083, 885. MS (ESI) $m/z$: 456.2 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{26}H_{31}FNO_3S^+$ $[M + H]^+$ 456.2003, found 456.1993.

*($R_S$,2S,3R)-2-Benzyl-2-fluoro-3-(2-methylpropane-2-sulfinylamino)-3-phenyl-propionic Acid Ethyl Ester (**9a**).* By following the general procedure, **9a** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (150 mg, 74%), mp 107.5−108.6 °C; $[\alpha]_D^{20}$ = −9.43 ($c$ = 0.55, $CHCl_3$); $^1H$ NMR (400 MHz,$CDCl_3$) δ = 7.36−7.54 (m, 5H), 7.21−7.27 (m, 3H), 7.06−7.18 (m, 2H), 4.79 (dd, $J$ = 25.6, 10.5 Hz, 1H), 4.01−4.10 (m, 3H), 2.99 (dd, $J$ = 39.3, 14.5 Hz, 1H), 2.46−2.80 (m, 1H), 1.18 (s, 9H), 1.09 (t, $J$ = 7.2 Hz, 3H); $^{19}F$ NMR (376 MHz, $CDCl_3$) δ = −177.82 (br); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ = 169.2 (d, $J$ = 25.6 Hz), 136.9, 133.6, 129.9, 128.8, 128.7, 128.5, 128.1, 127.2, 100.0 (d, $J$ = 199.1 Hz), 65.5 (d, $J$ = 18.8 Hz), 61.6, 56.5, 41.6, 41.4, 22.3, 13.9. IR ($cm^{-1}$): 3321, 2981, 1760, 1472, 1299, 1183, 1061, 871, 780. MS (ESI) $m/z$: 406.1 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{22}H_{29}FNO_3S^+$ $[M + H]^+$ 406.1847, found 406.1846.

*($R_S$,2S,3R)-2-Benzyl-3-(4-chloro-phenyl)-2-fluoro-3-(2-methylpropane-2-sulfinylamino)-propionic Acid Ethyl Ester (**9b**).* By following the general procedure, **9b** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (143 mg, 65%), mp 99−100 °C; $[\alpha]_D^{20}$ = +2.67 ($c$ = 0.57, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ = 7.33−7.48 (m, 4H), 7.18−7.25 (m, 3H), 7.08 (dd, $J$ = 4.3, 2.6 Hz, 2H), 4.74 (dd, $J$ = 25.2, 10.8 Hz, 1H), 3.88−4.17 (m, 3H), 2.96 (dd, $J$ = 39.3, 14.4 Hz, 1H), 2.65 (t, $J$ = 13.7 Hz, 1H), 1.15 (s, 9H), 1.05 (t, $J$ = 7.1 Hz, 3H); $^{19}F$ NMR (376 MHz, $CDCl_3$) δ = −177.55 (br); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ = 169.0 (d, $J$ = 25.4 Hz), 135.4, 134.8, 133.3, 129.9, 129.1, 128.2, 127.3, 99.8 (d, $J$ = 199.0 Hz), 64.8 (d, $J$ = 19.0 Hz), 61.8, 56.6, 41.4 (d, $J$ = 20.8 Hz), 22.3, 13.9. IR ($cm^{-1}$): 3327, 2956, 1730, 1496, 1367, 1139, 1095, 1014, 844. MS (ESI) $m/z$: 440.1 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{22}H_{28}ClFNO_3S^+$ $[M + H]^+$ 440.1451, found 440.1448.

*($R_S$,2S,3R)-2-Benzyl-2-fluoro-3-(2-methylpropane-2-sulfinylamino)-3-p-tolyl-propionic Acid Ethyl Ester (**9c**).* By following the general procedure, **9c** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (159 mg, 76%), mp 110−111 °C; $[\alpha]_D^{20}$ = −3.70 ($c$ = 0.52, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ = 7.32 (d, $J$ = 7.6 Hz, 2H), 7.12−7.25 (m, 5H), 7.09 (d, $J$ = 7.1 Hz, 2H), 4.72 (dd, $J$ = 26.0, 10.5 Hz, 1H), 4.01 (dd, $J$ = 14.6, 7.4 Hz, 2H), 2.57−3.12 (m, 2H), 2.35 (s, 3H), 1.14 (s, 9H), 1.06 (t, $J$ = 7.1 Hz, 3H); $^{19}F$ NMR (376 MHz, $CDCl_3$) δ = −177.8 (br); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ = 169.4, 138.5, 133.9, 133.7, 129.9, 129.6, 128.3, 128.1, 127.1, 100.1 (d, $J$ = 198.8 Hz), 65.3 (d, $J$ = 18.7 Hz), 61.6, 56.4, 41.4 (d, $J$ = 20.8 Hz), 22.3, 21.1, 13.9. IR ($cm^{-1}$): 3324, 2955, 2853, 1759, 1496, 1277, 1192, 1079, 856. MS (ESI) $m/z$: 420.2 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{23}H_{31}FNO_3S^+$ $[M + H]^+$ 420.1998, found 420.1994.

**Procedure for the Synthesis of the Fmoc-Protected α-Fluoro-β-amino Acid *tert*-Butyl Ester 10.** Into a 10 mL flask was placed **3a′** (171.5 mg, 0.5 mmol) and 1.25 N HCl/MeOH (1.0 mL). The reaction mixture was stirred at rt for 30 min and was then concentrated to near dryness. Diethyl ether was added to precipitate out the ammonium hydrochloride. The precipitate was suspended in a mixture of $CH_3CN$ (0.5 mL) and 10% $NaHCO_3$ (1.0 mL) at 0 °C. Then, a solution of 9-fluorenylmethyl *N*-succinimidyl carbonate (202 mg, 0.6 mmol) in $CH_3CN$ (0.5 mL) was added slowly. The resulting mixture was stirred at rt for 4 h, diluted with $H_2O$ (10 mL), and extracted three times with ethyl acetate (10 mL × 3). The combined organic layers were dried over anhydrous $MgSO_4$. Evaporation of the solvent under vacuum, followed by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1), gave the corresponding product **10**.

*(2S,3R)-3-(9H-Fluoren-9-ylmethoxycarbonylamino)-2-fluoro-3-phenyl-propionic Acid tert-Butyl Ester (**10**).* White solid (198 mg, 86%), mp 100.6−101.2 °C; $[\alpha]_D^{20}$ = +17.70 ($c$ = 0.53, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ = 7.79 (d, $J$ = 7.4 Hz, 2H), 7.59 (d, $J$ = 4.8 Hz, 2H), 7.30−7.46 (m, 9H), 5.74 (d, $J$ = 9.5 Hz, 1H), 5.41 (dd, $J$ = 28.7, 10.1 Hz, 1H), 5.09 (d, $J$ = 47.9 Hz, 1H), 4.31−4.58 (m, 3H), 4.23 (t, $J$ = 6.9 Hz, 1H), 1.48 (s, 9H).); $^{19}F$ NMR (376 MHz, $CDCl_3$) δ = −201.6 (dd, $J$ = 47.4, 28.7 Hz); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ = 166.2 (d, $J$ = 24.9 Hz), 155.5, 143.7, 143.6, 141.2, 137.4, 128.7, 128.1, 127.7, 127.0, 126.7, 125.0, 119.9, 90.3 (d, $J$ = 191.1 Hz), 83.8, 67.2, 55.8 (d, $J$ = 19.0 Hz), 47.1, 29.7, 27.8. IR ($cm^{-1}$): 3380, 3067, 2923, 1748, 1518, 1477, 1297, 1159, 1094, 842. MS (ESI) $m/z$: 479.2 $[M + NH_4]^+$. HRMS (ESI) $m/z$: calcd for $C_{28}H_{32}FN_2O_4^+$ $[M + NH_4]^+$ 479.2341, found 479.2332.

**Procedure for Synthesis of the Fmoc-Protected α-Fluoro-β-amino Acid 11.** In a 10 mL flask, TFA (0.9 mL) was added to a stirred solution of **10** (198 mg, 0.43 mmol) in DCM (2.0 mL) at rt, and the resulting mixture was stirred at rt for 16 h. Saturated $NaHCO_3$−$H_2O$ (10 mL) were then added, and the aqueous layer was extracted with DCM (10 mL × 2). The combined organic extracts were then concentrated under vacuum to give **11**.

*(2S,3R)-3-(9H-Fluoren-9-ylmethoxycarbonylamino)-2-fluoro-3-phenyl-propionic Acid (**11**).* White solid (146 mg, 84%), mp 186.1−186.7 °C; $[\alpha]_D^{20}$ = +13.36 ($c$ = 0.61, $CHCl_3$); $^1H$ NMR (400 MHz, *d*-DMSO) δ = 8.03 (d, $J$ = 8.0 Hz, 1H), 7.89 (d, $J$ = 8.0 Hz, 2H), 7.73−7.78 (m, 2H), 7.28−7.46 (m, 8H), 5.28 (dd, $J$ = 48.0, 4.0 Hz, 1H), 5.26 (dd, $J$ = 32.0, 8.0 Hz, 1H), 4.18−4.28 (m, 3H); $^{19}F$ NMR (376 MHz, $CDCl_3$) δ = −188.0 (br); $^{13}C$ NMR (101 MHz, *d*-DMSO) δ = 170.1(d, $J$ = 19.4 Hz), 155.8, 144.4, 144.0, 141.1, 141.0, 128.3, 128.0, 127.5, 127.2, 125.7, 125.6, 120.5, 92.5 (d, $J$ = 188.7 Hz), 66.0, 56.5 (d, $J$ = 21.6 Hz), 47.1. IR ($cm^{-1}$): 3386, 2936, 1752, 1683, 1528, 1477,



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1299, 1226, 1074, 977. MS (ESI) $m/z$: 406.1 $[M + H]^+$. HRMS (ESI) $m/z$: calcd for $C_{24}H_{21}FNO_4^+$ $[M + H]^+$ 406.1449, found 406.1442.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01574.

Copies of $^1H$, $^{19}F$, and $^{13}C$ NMR spectra of all new compounds
(PDF)

X-ray crystal structure of compound **3e′**
(CIF)

X-ray crystal structure of compound **9c**
(CIF)

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### Notes

The authors declare no competing financial interest.

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