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Diastereoselective Mannich Reactions Using Fluorinated Ketones: Synthesis of Stereogenic Carbon−Fluorine Units

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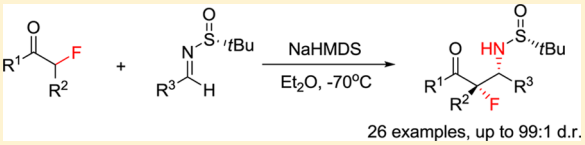
Supporting Information

ABSTRACT: A diastereoselective Mannich reaction of simple α-fluoro ketones with *N*-*tert*-butylsulfinylimines was developed. This method provides a concise route to a variety of structurally diverse α-fluoro-β-amino ketones containing fluorinated stereogenic carbon centers; good yields and high diastereoselectivities were achieved. This method uses readily accessible starting materials and has a broad substrate scope: cyclic and linear α-fluoro ketones and fluoromethyl ketones are all suitable substrates.



INTRODUCTION

Fluorine, which is small and the most electronegative element, has specific effects on the properties of organic molecules.[1] The introduction of fluorine into a bioactive molecule often improves the binding affinity, metabolic stability, and bioavailability.[2] Organofluorine compounds, therefore, play an integral role in life-science-related fields.[2] Among various fluorine-containing alkyl groups, stereogenic carbon−fluorine structural units are highly important because they commonly occur in many bioactive molecules and pharmaceuticals.[2,3]

Substantial effort has been devoted to the development of methods for the preparation of stereogenic carbon−fluorine units.[4,5] α-Fluoro ketones are important fluorocarbon nucleophiles and have been widely used in many asymmetric reactions.[6−9] The best results obtained have involved the use of doubly activated α-fluoro β-ketoesters,[7] fluorinated silyl enol ethers,[8] and/or 2-fluoro-1,3-diketo hydrates[9] as starting substrates. Although these reagents are efficient, the need for preactivation limits their general applicability. The direct construction of stereogenic carbon−fluorine units from simple fluorinated carbonyl compounds is an ideal alternative, considering that a wide variety of structurally diverse α-fluoro ketones can be readily obtained via the straightforward fluorination of ketones. However, because fluorine substitution has a dramatic impact on their reactivities,[1] the use of simple α-fluoro ketones in direct asymmetric reactions is challenging.[10] There are only a few literature reports that document the use of simple α-fluoro ketones in the construction of stereogenic carbon−fluorine structural units.[11,12] Trost, Tan, and others have shown that regular α-fluoro ketones can react with activated imines and alkyl halides enantioselectively to give α-fluorocarbonyl compounds.[11] However, these methods are limited to cyclic α-fluorocarbonyl substrates. The use of linear α-fluoro ketones in the asymmetric synthesis of carbon−fluorine units is even less common. Recently, Chen et al. reported an efficient Pd(0)-catalyzed allylic substitution of α-fluoro aromatic ketones to give enantioenriched tertiary α-fluorinated ketones.[12] They attributed the high enantiomeric excess to the generation of stereodefined enolates (Z/E > 20:1) under the reaction conditions used. Fluoromethyl ketones are the most challenging substrates; their use in direct asymmetric reactions has so far been limited to fluoroacetone. Direct asymmetric aldol reactions of aldehydes with fluoroacetone give stereogenic carbon−fluorine units,[13] but the analogous Mannich reactions, using fluoroacetone as the nucleophile, occur predominately at the nonfluorinated α-carbon.[14] The development of efficient direct asymmetric reactions of fluoro ketones is, therefore, important, particularly for linear and fluoromethyl substrates.

We have investigated the use of regular α-carbonyl compounds to construct stereogenic carbon−fluorine centers. Recently, we showed that α-fluorinated carboxylate esters are competent fluorocarbon nucleophiles and can be converted to α-fluoro-β-amino acid derivatives through highly diastereoselective Mannich reactions.[15] As part of our continuing investigation of the use of simple fluorocarbonyl compounds to construct carbon(sp^3)−fluorine centers, we have developed efficient Mannich reactions of α-fluoro ketones (including cyclic and linear α-fluoro ketones and fluoromethyl ketones) with Ellman's imines,[16] enabling access to β-amino ketones containing α-fluorinated stereogenic carbon centers (Scheme 1).

RESULTS AND DISCUSSION

We used α-fluorotetralone **1a** as a model substrate because we expected it to generate stereodefined enolates (Table 1). When **1a** was reacted with imine **2a** in THF with LiHMDS as a base, the reaction yielded the Mannich products **3aa** and **3aa′** with a ratio of 63:37 (entry 1). Changing the base to KHMDS or NaHMDS gave synthetically useful yields and high diastereoselectivities (entries 2 and 3). Other solvents were examined,

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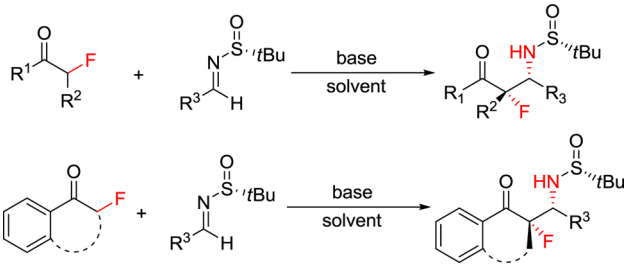
Scheme 1. Mannich Reactions of Fluoro Ketones with Ellman's Imines

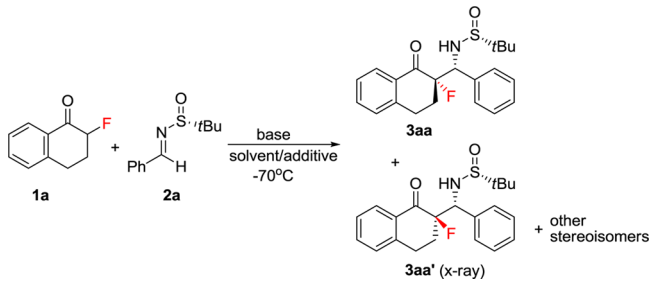


using NaHMDS as the base. Toluene and dioxane were not suitable for this reaction (entries 4 and 5), but improved yields were obtained when Et_2O was used (entry 6). Incorporation of additives such as CuCl, $ZnCl_2$, and $MgBr_2$ did not improve the reaction outcome (entries 7–9). An optimized reaction system consisting of **1a** (1.2 equiv), imine **2a** (1.0 equiv), and NaHMDS (1.2 equiv) in Et_2O at −70 °C afforded **3aa** in 76% yield with 92:5:3 diastereoselectivity (entry 10).

We then checked the substrate scope of the reaction in terms of the ketone. The data in Table 2 show that various structurally diverse α-fluoro ketones were successfully reacted with imine **2a** using the optimized reaction conditions. Six-membered (2-fluoro-1-tetralone **1a**, 3-fluoro-4-chromanone **1b**, and 5-fluoro-6,7-dihydrobenzo[*b*]thiophenone **1c**), seven-membered (2-fluoro-1-benzosuberone **1d**), and five-membered (2-fluoro-1-indanone **1e**) (hetero)cyclic ketones were the best substrates and gave the Mannich products **3aa**–**3ea** in good to excellent yields with high diastereoselectivities (>90:10). Notably, the 1-fluoro-2-indanone **1f** reacted regioselectively at the fluorine-substituted α-position to give the major stereoisomer **3fa** in a synthetically useful yield (65%) and diastereoselectivity (82:6:5:7). The regioselectivity of the reaction indicates that the C(F)–H bond is more acidic and the resultant fluoroenolate is kinetically much more reactive. It is interesting to note that, in the proline-catalyzed Mannich reactions employing fluoroacetone as donor, attack of the methyl group, rather than the fluoromethyl group of fluoroacetone, results in the formation of the α′-fluoro β-amino ketones as the major Mannich products through the thermodynamically more stable enamine with the less-substituted double bond (rather than the enamine with the fluorine-substituted double bond).[14] Linear ketones (α-fluoropropiophenone **1g**, 1-adamantyl fluoromethyl ketone **1h**, 2-fluoro-1-*o*-tolylethanone **1i**, 2-fluoro-1-(2-methoxyphenyl)-ethanone **1j**) could also be used as substrates and were efficient under these conditions. α-Fluoropropiophenone **1g** reacted smoothly with the methyl-substituted imine **2b** to give the corresponding product **3gb** containing a quaternary fluorinated carbon center in 75% yield and with 82:18 diastereoselectivity. Fluoromethyl ketones were also competent substrates for this transformation; 1-adamantyl fluoromethyl ketone **1h** and *ortho*-methyl and *ortho*-methoxyl substrates (**1i**, **1j**) gave the products **3ha**, **3ib**, and **3jb**, all with high diastereoselectivities. *meta*-methyl and *meta*-methoxy substrates (**1k**, **1l**) and fluoromethyl phenyl ketone **1m** were also examined. However, very low diastereoselectivities were obtained (34:33:33 d.r. for **1k**, 46:46:8 d.r. for **1l** and 34:33:33 d.r. for **1m**). These results suggest that an ortho substituent has an important effect on the stereochemical outcome of the reaction. Aliphatic α-fluoroketones with two different kinds of α-protons such as fluoroacetone and 2-fluorocyclohexanone were not competent nucleophiles; complex reaction mixtures were afforded.

Next, we explored other imines for this reaction (Table 3). The reaction proceeded smoothly with cyclic α-fluoro ketones and imines bearing electron-donating (alkoxy and alkyl) and electron-withdrawing groups (chloro) to give the Mannich products in good yields and with high diastereoselectivities (**3ab**, **3ac**, and **3ad**). The heteroaromatic 2-furanyl substrate **2e** gave **3ae** in 83% yield and with 90:10 diastereoselectivity. As

Table 1. Optimization of the Addition of α-Fluoroketone 1a to Imine 2a



entry	**1a**/**2a**/base	base	solvent/additive[a]	yield[b] (%)	d.r.[c] (**3aa**:**3aa′**:others)
1	1.0:1.0:1.0	LiHMDS	THF	42	63:37:0:0
2	1.0:1.0:1.0	KHMDS	THF	60	82:15:3:0
3	1.0:1.0:1.0	NaHMDS	THF	61	89:6:3:2
4	1.0:1.0:1.0	NaHMDS	toluene	48	83:11:6:0
5	1.0:1.0:1.0	NaHMDS	1,4-dioxane	30	N[d]
6	1.0:1.0:1.0	NaHMDS	Et_2O	66	91:3:3:3
7	1.0:1.0:1.0	NaHMDS	Et_2O/CuCl	52	N[d]
8	1.0:1.0:1.0	NaHMDS	Et_2O/$ZnCl_2$	58	85:7:5:3
9	1.0:1.0:1.0	NaHMDS	Et_2O/$MgBr_2$	62	88:5:4:3
10	1.2:1.0:1.2	NaHMDS	Et_2O	76	92:5:3:0

[a]A combination of 0.2 mmol of additive $ZnCl_2$ or $MgBr_2$ and 1.5 mL of THF was used on a 0.5 mmol scale (for **2a**). [b]Yields refer to isolated yields of the major stereoisomers. [c]d.r. determined by ^{19}F NMR spectroscopy. [d]Not determined.

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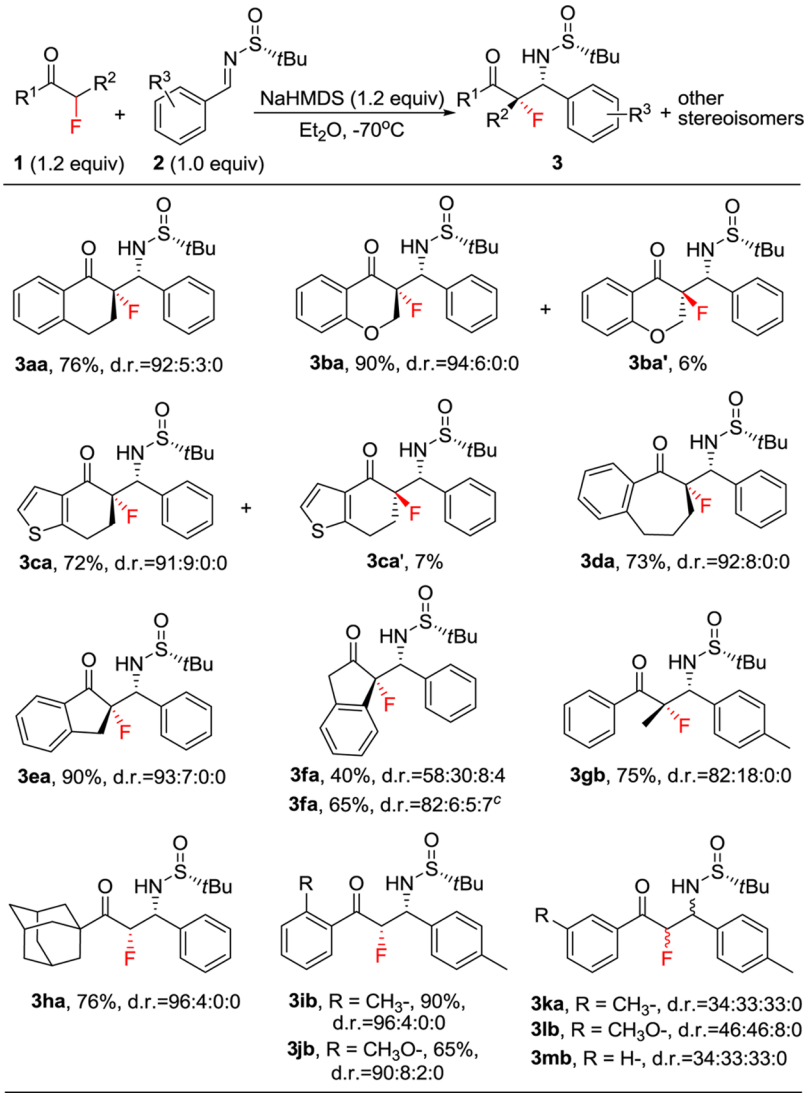
Table 2. Scope of Reaction Using α-Fluoro Ketone Substrates[a,b]



[a]The yields refer to isolated yields of the major stereoisomers. [b]d.r. determined by ^{19}F NMR spectroscopy. [c]KHMDS was used instead of NaHMDS in this process.

well as (hetero)aromatic imines, the α,β-unsaturated substrate **2f** participated in this reaction, leading to product **3af**, with a diastereoselectivity of 99:1. Even the aliphatic butyr- and isovaleraldehyde sulfinyl imines (**2g** and **2h**), which tend to undergo enolization under strongly basic conditions, were well tolerated and gave the corresponding products **3bg** and **3bh** in good yields. Mannich reactions between linear α-fluoro ketones and imines were further examined. The reaction of α-fluoropropiophenone **1g** with chloro-substituted imine **2d** gave **3gd** in 83% yield and with 91:9 diastereoselectivity, i.e., reactivity and stereoselectivity comparable to those of the methyl-substituted imine **2b** (Table 2, **3gb**). When aliphatic fluoromethyl ketone **1h** was used in the reaction, imines with alkyl (**2b**), bromo (**2i**), ester (**2j**), nitro (**2k**), or nitrile (**2l**) groups were all tolerated, invariably leading to the target products (**3hb**, **3hi**−**3hl**), with excellent diastereoselectivities. The reaction of *ortho*-methoxyfluoroacetophenone **1j** with 4-bromo imine substrate (**2i**) gave the desired product **3ji** in 75% yield and with 88:7:4:1 diastereoselectivity. Lastly, fluoropinacolone **1n** was also successfully used, giving the Mannich product **3na** in an isolated yield of 70%. The configurations of **3ad** and **3na** were confirmed using X-ray crystallography,[17] and by analogy, the same configuration was assigned to all major diastereoisomers **3**. The observed stereochemical outcome of the reaction can be explained by a chairlike transition state (Figure 1a), which has been suggested by Davis, Ellman, and other researchers to be involved in condensation reactions of metal enolates and imines.[16,18] The *Z*-fluoroenolates of the α-fluoro ketones are believed to participate in the process; they attack the *Si* face of (*R*)-*N*-*tert*-butylsulfinylimines, providing access to the major *syn* diastereoisomers. The absolute configuration of **3aa′** was established by X-ray crystallographic analysis, and by analogy, the same configuration was assigned to **3ba′** and **3ca′**. A boatlike transition state is proposed to explain the formation of the minor *anti* diastereoisomers, where the *Z*-fluoroenolates of the α-fluoro ketones approach the *Si* face of (*R*)-sulfinylimines (Figure 1b).

The *t*BuS(O) group can be easily removed following reported procedures; for example, treatment of **3hi** with MeOH/HCl gave the corresponding ammonium salt which, without purification, further reacted with Boc_2O to give the N-Boc product **4** in 91% yield (Scheme 2). No racemization

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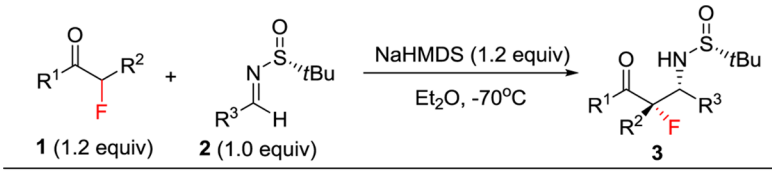
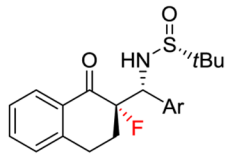
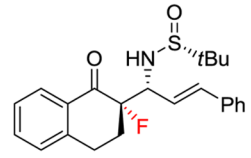
Table 3. Scope of Reaction of α-Fluoro Ketones and Imines[a,b]

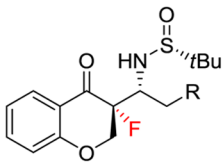




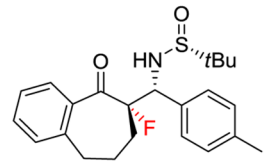
3ab, Ar= 4-$CH_3C_6H_4$, 67%, d.r.=93:7:0:0
3ac, Ar= 2-$CH_3OC_6H_4$, 88%, d.r.=96:4:0:0
3ad, Ar= 4-ClC_6H_4, 86%, d.r.=89:7:4:0 (x-ray)
3ae, Ar= 2-furanyl, 83%, d.r.=90:10:0:0



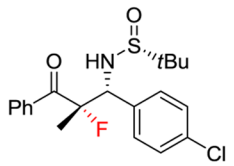
3af, 76%, d.r.>99:1:0:0



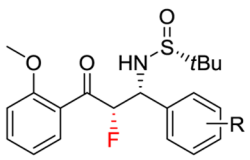
3bg, R = *n*-C_2H_5, 73%, d.r.=90:10:0:0
3bh, R = *i*-C_3H_7, 76%, d.r.=86:8:6:0



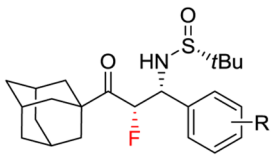
3db, 80%, d.r.=96:4:0:0



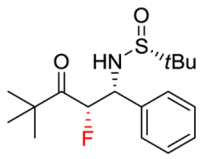
3gd, 83%, d.r.=91:9:0:0



3ji, R= 4-Br, 75%, d.r.=88:7:4:1



3hb, R= 4-CH_3,74%, d.r.=99:1:0:0
3hi, R= 4-Br, 81%, d.r.=99:1:0:0
3hj, R= 4-CO_2CH_3, 73%, d.r.=99:1:0:0
3hk, R= 4-NO_2, 89%, d.r.=99:1:0:0
3hl, R= 4-CN, 81%, d.r.=99:1:0:0



3na, 70%, d.r.=91:9:0:0 (x-ray)

[a]The yields refer to isolated yields of the major stereoisomers. [b]d.r. determined by ^{19}F NMR spectroscopy.

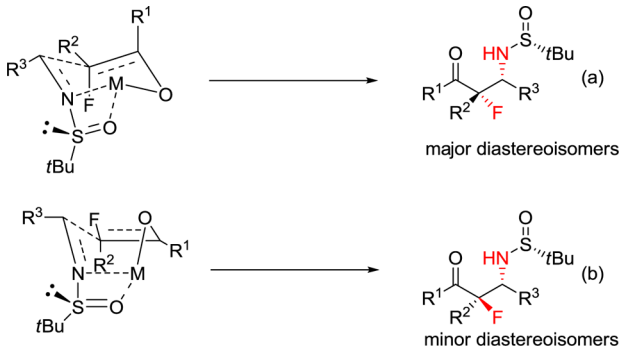
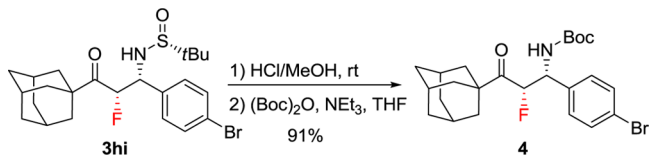


Figure 1. (a) Closed transition-state mode proposed for addition of α-fluoro ketone and Ellman's imine to give *syn* diastereoisomers. (b) Boatlike transition-state mode proposed for addition of α-fluoro ketone and Ellman's imine to give *anti* diastereoisomers.

occurred during the process, suggesting that the fluorinated α-carbon center is robust under mild acidic or basic conditions.

Scheme 2. Removal of Sulfinyl Group of 3hi



CONCLUSIONS

We have developed a highly diastereoselective Mannich reaction of fluoro ketones. This reaction provides an efficient method for the preparation of α-fluoro-β-amino ketones containing fluorinated stereogenic carbon centers. The reaction has a broad substrate scope: cyclic, acyclic, and even fluoromethyl ketones can be successfully used in the reaction. We believe that this synthetic method will enable robust syntheses of a wide variety of fluorinated compounds with stereogenic carbon−fluorine units.

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EXPERIMENTAL SECTION

Unless otherwise mentioned, all commercial reagents and solvents were used directly as purchased. Compounds **2** were prepared according to literature methods.[11a,19] The ether was dried with molecular sieves before use. Flash chromatography was performed on silica gel with petroleum ether/ethyl acetate as the eluent. Melting points were uncorrected. Optical rotations were measured with a sodium lamp. ^{1}H, ^{13}C, and ^{19}F 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 (δ) are reported in parts per million (ppm), and coupling constants (J) are given in hertz (Hz). IR spectra were recorded on an FT-IR spectrometer by using KBr pellets. HRMS data using ESI were obtained on an ESI-FTMS mass spectrometer.

Typical Procedure for the Diastereoselective Addition of Fluoroketone 1 to *N*-*tert*-Butylsulfinyl Imine 2. Under a N_2 atmosphere, NaHMDS (1.2 equiv, 0.6 mL, 1.0 mol/L in THF) was added slowly to a mixture of fluoroketone **1** (0.6 mmol, 1.2 equiv), imine **2** (0.5 mmol, 1.0 equiv), and ethyl ether (1.5 mL) at −70 °C. Reaction mixtures were stirred at this temperature for 30 min. Then, 1 N TFA/THF (2 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**.

*(Rs)-N-[(R)-((S)-2-Fluoro-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methyl]-2-methylpropane-2-sulfinamide (**3aa**).* By following the general procedure, **3aa** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (142 mg, 76%), mp 110−112 °C; $[\alpha]_D^{20}$ = −77.8 (c = 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.10 (d, J = 7.6 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.46 (d, J = 5.0 Hz, 2H), 7.31−7.40 (m, 4H), 7.24 (d, J = 3.8 Hz, 1H), 4.80 (d, J_{HCCF} = 23.6 Hz, 1H), 4.77 (s, 1H), 2.93−3.12 (m, 2H), 2.20−2.37 (m, 1H), 1.88−2.04 (m, 1H), 1.18 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −172.2 (dt, J = 23.3, 11.8 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.8 (d, J = 18.1 Hz), 142.5, 136.0, 134.7, 130.6, 129.7, 129.0, 128.7, 128.6, 128.5, 127.4, 95.2 (d, J_{CF} = 193.4 Hz), 58.7 (d, J = 19.2 Hz), 55.8, 31.0 (d, J = 21.7 Hz), 25.4 (d, J = 10.1 Hz), 22.6. IR (cm^{-1}): 2959, 2905, 1713, 1688, 1504, 1454, 1342, 1100, 906, 743. MS (ESI) m/z: 374.2 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{21}H_{25}FNO_2S^+$ $[M + H]^+$ 374.1585, found 374.1585.

*(Rs)-N-[(R)-((R)-2-Fluoro-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methyl]-2-methylpropane-2-sulfinamide (**3aa′**).* Under a N_2 atmosphere, KHMDS (1.2 equiv, 1.2 mL, 1.0 mol/L in THF) was added to a mixture of α-fluorotetralone **1a** (1.2 mmol, 1.2 equiv), imine **2a** (1 mmol, 1.0 equiv), and THF (1.5 mL) at −70 °C. Reaction mixtures were stirred at this temperature for 30 min. Then, 1 N TFA/THF (2 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 (petroleum ether/ethyl acetate = 3/1), gave **3aa′** as a white solid (38 mg, 10%), mp 172−174 °C; $[\alpha]_D^{20}$ = −87.8 (c = 0.55, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.86 (d, J = 7.8 Hz, 1H), 7.55 (td, J = 7.6, 1.2 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.30−7.24 (m, 4H), 7.18−7.04 (m, 2H), 4.82 (dd, J = 21.4 (J_{HCCF}), 6.7 Hz, 1H), 4.48 (d, J = 6.5 Hz, 1H), 3.43−2.99 (m, 2H), 2.77−2.83 (m, 1H), 2.65−2.35 (m, 1H), 1.20 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −166.7 (dd, J = 20.8, 10.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 192.8 (d, J = 17.2 Hz), 142.3, 136.5, 134.2, 131.9, 128.9, 128.4, 128.4, 128.3, 128.0, 127.2, 96.9 (d, J_{CF} = 191.0 Hz), 61.9 (d, J = 22.1 Hz), 56.3, 30.7 (d, J = 21.6 Hz), 25.7 (d, J = 10.4 Hz), 22.4. IR (cm^{-1}): 2948, 1706, 1604, 1436, 1364, 1094, 1071, 773, 816, 716, 701. MS (ESI) m/z: 374.2 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{21}H_{25}FNO_2S^+$ $[M + H]^+$ 374.1585, found 374.1588.

*(Rs)-N-[(R)-((R)-3-Fluoro-4-oxochroman-3-yl)(phenyl)methyl]-2-methylpropane-2-sulfinamide (**3ba**).* By following the general procedure, **3ba** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a pale yellow oily liquid (169 mg, 90%); $[\alpha]_D^{20}$ = −4.2 (c = 0.40, CH_3OH); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.99 (dd, J = 7.9, 1.5 Hz, 1H), 7.53−7.60 (m, 1H), 7.46−7.51 (m, 2H), 7.36−7.44 (m, 3H), 7.13 (t, J = 7.4 Hz, 1H), 7.01 (d, J = 8.4 Hz, 1H), 4.93 (dd, J = 25.2 (J_{HCCF}), 1.7 Hz, 1H), 4.73 (s, 1H), 4.22 (dd, J = 12.0, 6.6 Hz, 1H), 4.09 (dd, J = 11.9, 7.6 Hz, 1H), 1.22 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −187.5 (d, J = 25.1 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 189.0 (d, J = 17.7 Hz), 161.0, 137.4, 134.5, 129.7, 129.1, 128.6, 128.5, 122.8, 119.1, 117.9, 90.9 (d, J_{CF} = 197.3 Hz), 69.4 (d, J = 30.5 Hz), 57.9 (d, J = 19.0 Hz), 56.0, 22.6. IR (cm^{-1}): 2911, 1703, 1595, 1466, 1364, 1068, 1015, 928, 816, 762. MS (ESI) m/z: 376.1 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{20}H_{23}FNO_3S^+$ $[M + H]^+$ 376.1377, found 376.1380.

*(Rs)-N-[(R)-((S)-3-Fluoro-4-oxochroman-3-yl)(phenyl)methyl]-2-methylpropane-2-sulfinamide (**3ba′**).* By following the general procedure (1.0 mmol scale), **3ba′** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a sticky oil (23 mg, 6.0%); $[\alpha]_D^{20}$ = −5.6 (c = 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.77 (d, J = 7.2 Hz, 1H), 7.53 (t, J = 7.2 Hz, 1H), 7.29−7.20 (m, 4H), 7.11 (d, J = 7.8 Hz, 2H), 6.98 (d, J = 8.4 Hz, 1H), 5.08−4.87 (m, 2H), 4.42−4.47 (m, 2H), 1.19 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −180.5 (d, J = 20.6 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 187.6 (d, J = 17.1 Hz), 160.5, 136.8, 135.3, 128.7, 128.3, 128.1, 127.4, 122.4, 120.1, 118.0, 92.3 (d, J_{CF} = 202.1 Hz), 69.4 (d, J = 31.4 Hz), 61.3 (d, J = 21.2 Hz), 56.4, 22.4. IR (cm^{-1}): 2924, 1709, 1607, 1475, 1214, 1073, 1039, 948, 850, 782. MS (ESI) m/z: 376.1 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{20}H_{23}FNO_3S^+$ $[M + H]^+$ 376.1377, found 376.1377.

*(Rs)-N-[(R)-((S)-5-Fluoro-4-oxo-4,5,6,7-tetrahydrobenzo[b]-thiophen-5-yl)(phenyl)methyl]-2-methylpropane-2-sulfinamide (**3ca**).* By following the general procedure, **3ca** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (136 mg, 72%), m.p.160−162 °C; $[\alpha]_D^{20}$ = −100.0 (c = 0.38, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.48 (d, J = 5.0 Hz, 2H), 7.44 (d, J = 5.3 Hz, 1H), 7.39 (dd, J = 5.5, 3.5 Hz, 3H), 7.16 (d, J = 5.3 Hz, 1H), 4.88 (s, 1H), 4.85 (d, J_{HCCF} = 21.8 Hz, 1H), 3.05−3.13 (m, 2H), 2.37 (tt, J = 11.2, 7.4 Hz, 1H), 2.03 (tt, J = 15.0, 4.9 Hz, 1H), 1.22 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −174.2 (*br*). ^{13}C NMR (101 MHz, $CDCl_3$) 187.9 (d, J = 18.9 Hz), 155.3, 136.0, 135.3, 129.8, 128.8, 128.5, 125.7, 125.3, 95.0 (d, J_{CF}= 193.2 Hz), 59.1 (d, J = 19.2 Hz), 55.8, 32.4 (d, J = 22.8 Hz), 22.6, 22.4. IR (cm^{-1}): 2966, 1671, 1527, 1409, 1364, 1255, 1069, 996, 835, 794. MS (ESI) m/z: 380.1 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{19}H_{23}FNO_2S_2^+$ $[M + H]^+$ 380.1149, found 380.1151.

*(Rs)-N-[(R)-((R)-5-Fluoro-4-oxo-4,5,6,7-tetrahydrobenzo[b]-thiophen-5-yl)(phenyl)methyl]-2-methylpropane-2-sulfinamide (**3ca′**).* By following the general procedure (1.0 mmol scale), **3ca′** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (26 mg, 7%), mp 165−168 °C; $[\alpha]_D^{20}$ = −86.8 (c = 0.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.44−7.36 (m, 1H), 7.32 (d, J = 5.3 Hz, 1H), 7.28 (d, J = 4.5 Hz, 2H), 7.16 (d, J = 5.5 Hz, 3H), 4.84 (dd, J = 18.7 (J_{HCCF}), 5.9 Hz, 1H), 4.58 (d, J = 5.6 Hz, 1H), 3.15 (td, J = 13.0, 6.3 Hz, 1H), 3.04−2.92 (m, 1H), 2.77 (tt, J = 13.5, 4.8 Hz, 1H), 2.61−2.45 (m, 1H), 1.20 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −164.21 − −165.06 (m). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 186.8 (d, J = 18.7 Hz), 154.9, 136.4 (d, J = 11.7 Hz), 128.9, 128.6, 128.5, 128.3, 125.3, 125.0, 96.1 (d, J_{CF} = 189.3 Hz), 62.9 (d, J = 23.0 Hz), 56.2, 32.4 (d, J = 23.0 Hz), 22.6, 22.5. IR (cm^{-1}): 2987, 1700, 1528, 1400, 1364, 1228, 1075, 986, 831, 756. MS (ESI) m/z: 380.1 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{19}H_{23}FNO_2S_2^+$ $[M + H]^+$ 380.1149, found 380.1152.

*(Rs)-N-[(R)-((S)-2-Fluoro-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)(phenyl)methyl]-2-methylpropane-2-sulfinamide (**3da**).* By following the general procedure, **3da** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a pale yellow liquid (141 mg, 73%); $[\alpha]_D^{20}$ = −40.4 (c = 0.26, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57−7.68 (m, 1H), 7.41 (td, J = 7.5, 1.2 Hz, 1H), 7.29−7.38 (m, 6H), 7.20 (d, J = 7.5 Hz, 1H), 5.00 (dd, J = 21.8 (J_{HCCF}), 7.1 Hz, 1H), 4.30 (d, J = 7.0 Hz, 1H), 3.15 (dd, J = 16.1, 10.4 Hz, 1H), 2.93 (dd, J = 16.6, 7.3 Hz, 1H), 1.72−1.77 (m, 2H), 1.21−1.37 (m, 2H), 1.13 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −166.8 (*br*). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 203.8 (d,

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J = 29.9 Hz), 141.3, 137.2, 136.9, 131.5, 129.2, 129.1, 129.0, 128.4, 128.2, 126.6, 104.2 (d, J_{CF} = 190.8 Hz), 63.0 (d, J = 20.3 Hz), 56.1, 34.6 (d, J = 21.8 Hz), 33.5, 23.5, 22.4. IR (cm^{-1}): 2949, 1668, 1457, 1364, 1291, 1191, 1076, 997, 877, 729. MS (ESI) m/z: 410.2 $[M + Na]^+$. HRMS (ESI) m/z: calcd for $C_{22}H_{26}FNNaO_2S^+$ $[M + Na]^+$ 410.1560, found 410.1556.

*(Rs)-N-[(R)-((S)-2-Fluoro-1-oxo-2,3-dihydro-1H-inden-2-yl)(phenyl)methyl]-2-methylpropane-2-sulfinamide (**3ea**).* By following the general procedure, **3ea** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a colorless liquid (162 mg, 90%); $[\alpha]_D^{20}$ = −133.3 (c = 0.26, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.67 (d, J = 7.7 Hz, 1H), 7.46 (t, J = 7.4 Hz, 1H), 7.26−7.35 (m, 2H), 7.22 (dd, J = 6.2, 2.9 Hz, 2H), 7.10−7.15 (m, 3H), 5.01 (dd, J = 11.2, 2.8 Hz, 1H), 4.77 (s, 1H), 3.23−3.52 (m, 2H), 1.21 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −158.8 − −159.1 (m). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 199.3 (d, J = 18.7 Hz), 149.7 (d, J = 4.7 Hz), 136.3, 135.0, 134.9 (d, J = 6.1 Hz), 128.9, 128.6, 128.4, 128.2, 126.2, 124.2, 97.4 (d, J_{CF} = 195.3 Hz), 63.4 (d, J = 25.0 Hz), 56.1, 37.0 (d, J = 23.6 Hz), 22.5. IR (cm^{-1}): 2962, 1720, 1604, 1585, 1451, 1303, 1100, 912, 765. MS (ESI) m/z: 360.1 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{20}H_{23}FNO_2S^+$ $[M + H]^+$ 360.1428, found 360.1424.

*(Rs)-N-[(R)-((S)-1-Fluoro-2-oxo-2,3-dihydro-1H-inden-1-yl)(phenyl)methyl]-2-methylpropane-2-sulfinamide (**3fa**).* By following the general procedure (KHMDS was used in this case), **3fa** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a colorless liquid (117 mg, 65%); $[\alpha]_D^{20}$ = −153.7 (c = 0.29, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.69 (d, J = 7.7 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.33 (d, J = 7.3 Hz, 1H), 7.23 (dd, J = 6.5, 3.0 Hz, 2H), 7.16 (dd, J = 7.5, 4.9 Hz, 4H), 5.02 (dd, J = 11.4, 2.8 Hz, 1H), 4.73 (s, 1H), 3.46−3.53 (m, 1H), 3.29−3.40 (m, 1H), 1.24 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −159.9 (*br*). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 199.3 (d, J = 18.8 Hz), 149.6 (d, J = 4.7 Hz), 136.2, 135.0, 134.9 (d, J = 6.2 Hz), 128.9, 128.6, 128.2, 128.1, 126.1, 124.3, 97.4 (d, J_{CF} = 195.3 Hz), 63.45 (d, J = 24.9 Hz), 56.2, 37.0 (d, J = 23.6 Hz), 22.6. IR (cm^{-1}): 2966, 1722, 1585, 1450, 1310, 1125, 903, 773, 765. MS (ESI) m/z: 360.1 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{20}H_{23}FNO_2S^+$ $[M + H]^+$ 360.1428, found 360.1425.

*(Rs)-N-[(1R,2S)-2-Fluoro-2-methyl-3-oxo-3-phenyl-1-(p-tolyl)propyl]-2-methylpropane-2-sulfinamide (**3gb**).* By following the general procedure, **3gb** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a pale yellow liquid (141 mg, 75%); $[\alpha]_D^{20}$ = −68.7 (c = 0.32, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.83−7.95 (m, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.40 (t, J = 7.7 Hz, 2H), 7.12−7.18 (m, 4H), 4.95 (dd, J = 18.3 (J_{HCCF}), 6.0 Hz, 1H), 4.43 (d, J = 5.8 Hz, 1H), 2.33 (s, 3H), 1.63 (d, J_{HCCF} = 22.4 Hz, 3H), 1.14 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −159.5 (d, J = 21.2 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 201.3 (d, J = 26.4 Hz), 138.1, 135.2 (d, J = 3.8 Hz), 133.6, 133.3, 129.8 (d, J = 8.1 Hz), 129.0, 128.9 (d, J = 1.4 Hz), 128.2 (d, J = 21.0 Hz), 102.9 (d, J_{CF} = 193.6 Hz), 64.3 (d, J = 21.7 Hz), 56.1, 22.9 (d, J = 23.2 Hz), 22.5, 21.1. IR (cm^{-1}): 2956, 1637, 1444, 1364, 1274, 1181, 1069, 983, 839, 714. MS (ESI) m/z: 376.2 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{21}H_{27}FNO_2S^+$ $[M + H]^+$ 376.1741, found 376.1743.

*(Rs)-N-[(1R,2S)-3-Adamantanyl-2-fluoro-3-oxo-1-phenylpropyl]-2-methylpropane-2-sulfinamide (**3ha**).* By following the general procedure, **3ha** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a liquid (154 mg, 76%), mp 113 °C; $[\alpha]_D^{20}$ = −48.7 (c = 0.43, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.30 (s, 5H), 5.30 (dd, J = 45.0 (J_{HCF}), 7.5 Hz, 1H), 4.90 (dd, J = 16.0, 5.8 Hz, 1H), 4.64 (s, 1H), 1.87−1.92 (m, 3H), 1.48−1.69 (m, 12H), 1.21 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −187.3 (d, J = 46.9 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 204.1 (d, J = 16.0 Hz), 131.1, 124.0, 123.9, 123.8, 86.0 (d, J_{CF} = 190.1 Hz), 54.4 (d, J = 19.9 Hz), 51.4, 41.9, 31.6, 31.4, 22.6 (d, J = 12.3 Hz), 17.8 (d, J = 35.2 Hz). IR (cm^{-1}): 2907, 1700, 1556, 1457, 1351, 1162, 1047, 993, 730. MS (ESI) m/z: 406.2 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{23}H_{33}FNO_2S^+$ $[M + H]^+$ 406.2211, found 406.2208.

*(Rs)-N-[(1R,2S)-2-Fluoro-3-oxo-3-(o-tolyl)-1-(p-tolyl)propyl]-2-methylpropane-2-sulfinamide (**3ib**).* By following the general procedure, **3ib** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a colorless liquid (169 mg, 90%); $[\alpha]_D^{20}$ = −47.3 (c = 0.30, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.42 (d, J = 8.1 Hz, 1H), 7.37 (dd, J = 11.2, 3.8 Hz, 1H), 7.20 (dd, J = 13.5, 7.4 Hz, 4H), 7.12 (d, J = 8.0 Hz, 2H), 5.72 (dd, J = 48.0 (J_{HCF}), 5.4 Hz, 1H), 4.98 (dt, J = 16.2, 5.1 Hz, 1H), 4.44 (d, J = 3.9 Hz, 1H), 2.32 (s, 6H), 1.25 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −187.8 (dd, J = 48.0, 16.2 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 198.8 (d, J = 20.6 Hz), 139.2, 138.42, 135.1, 133.2, 132.1, 131.9, 129.3, 128.8 (d, J = 4.6 Hz), 128.2, 125.4, 94.6 (d, J_{CF} = 193.2 Hz), 59.4 (d, J = 20.0 Hz), 56.0, 22.6, 21.1, 20.6. IR (cm^{-1}): 2901, 1706, 1678, 1476, 1313, 1201, 1137, 1096, 919, 765. MS (ESI) m/z: 398.1 $[M + Na]^+$. HRMS (ESI) m/z: calcd for $C_{21}H_{26}FNaNO_2S^+$ $[M + Na]^+$ 398.1560, found 398.1556.

*(Rs)-N-[(1R,2S)-2-fluoro-3-(2-methoxyphenyl)-3-oxo-1-p-tolylpropyl]-2-methylpropane-2-sulfinamide (**3jb**).* By following the general procedure, **3jb** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a colorless liquid (127 mg, 65%); $[\alpha]_D^{20}$ = −52.1 (c = 0.51, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.74 (dd, J = 7.7, 1.5 Hz, 1H), 7.66−7.44 (m, 1H), 7.29 (d, J = 7.7 Hz, 2H), 7.16 (d, J = 7.9 Hz, 2H), 7.05 (t, J = 7.5 Hz, 1H), 6.96 (d, J = 8.4 Hz, 1H), 6.02 (dd, J = 47.9 (J_{HCF}), 3.2 Hz, 1H), 4.93 (d, J_{HCCF} = 22.3 Hz, 1H), 4.34 (s, 1H), 3.93 (s, 3H), 2.35 (s, 3H), 1.21 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −199.3 (*br*). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 158.4, 138.1, 134.9, 131.6, 129.2, 128.0, 125.1, 121.3, 111.3, 95.8 (d, J_{CF} = 190.0 Hz), 58.3 (d, J = 18.7 Hz), 56.0, 55.6, 22.6, 21.1. IR (cm^{-1}): 2955, 1690, 1485, 1463, 1239, 1181, 1069, 899, 758. MS (ESI) m/z: 392.1 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{21}H_{27}FNO_3S^+$ $[M + H]^+$ 392.1690, found 392.1694.

*(Rs)-N-[(R)-((S)-2-Fluoro-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)(p-tolyl)methyl]-2-methylpropane-2-sulfinamide (**3ab**).* By following the general procedure, **3ab** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (130 mg, 67%), mp 153−155 °C; $[\alpha]_D^{20}$ = −62.6 (c = 0.39, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.11 (d, J = 7.9 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.37 (t, J = 7.5 Hz, 3H), 7.18−7.26 (m, 3H), 4.65−4.87 (m, 2H), 2.93−3.14 (m, 2H), 2.37 (s, 3H), 2.21−2.34 (m, 1H), 1.96−2.01 (m, 1H), 1.20 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −172.1 − −172.4 (m). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.9 (d, J = 17.9 Hz), 142.6, 138.6, 134.7, 132.8, 130.7, 129.6, 129.2, 129.0, 128.6, 127.4, 95.3 (d, J_{CF} = 193.1 Hz), 58.4 (d, J = 19.3 Hz), 55.8, 31.1 (d, J = 21.6 Hz), 25.4 (d, J = 10.0 Hz), 22.6, 21.2. IR (cm^{-1}): 2949, 1681, 1505, 1456, 1223, 1159, 1050, 880, 746. MS (ESI) m/z: 388.2 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{22}H_{27}FNO_2S^+$ $[M + H]^+$ 388.1741, found 388.1742.

*(Rs)-N-[(R)-((S)-2-Fluoro-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)(2-methoxyphenyl)methyl]-2-methylpropane-2-sulfinamide (**3ac**).* By following the general procedure, **3ac** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (177 mg, 88%), mp 157−158 °C; $[\alpha]_D^{20}$ = −72.3 (c = 0.56, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.13 (d, J = 7.9 Hz, 1H), 7.51−7.58 (m, 2H), 7.28−7.40 (m, 2H), 7.23 (d, J = 7.6 Hz, 1H), 7.01 (t, J = 7.5 Hz, 1H), 6.93 (d, J = 8.3 Hz, 1H), 5.44 (d, J_{HCCF} = 27.0 Hz, 1H), 4.93 (s, 1H), 3.84 (s, 3H), 3.24−3.40 (m, 1H), 2.91 (d, J = 17.5 Hz, 1H), 2.14−2.27 (m, 1H), 1.95−2.07 (m, 1H), 1.16 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −171.1 − −171.6 (m). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 194.71 (d, J = 18.1 Hz), 157.7, 143.2, 134.6, 131.4 (d, J = 4.3 Hz), 130.9, 129.5, 129.1, 128.4, 127.2, 124.6, 121.0, 110.7, 96.1 (d, J_{CF} = 193.6 Hz), 55.8 (d, J = 3.6 Hz), 51.1, 50.9, 31.8 (d, J = 21.3 Hz), 25.3 (d, J = 10.4 Hz), 22.6. IR (cm^{-1}): 2953, 1703, 1596, 1460, 1226, 1175, 1085, 906, 748. MS (ESI) m/z: 404.2 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{22}H_{27}FNO_3S^+$ $[M + H]^+$ 404.1690, found 404.1685.

*(Rs)-N-[(R)-(4-Chlorophenyl)((S)-2-fluoro-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)methyl]-2-methylpropane-2-sulfinamide (**3ad**).* By following the general procedure, **3ad** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (175 mg, 86%), mp 175−176 °C; $[\alpha]_D^{20}$ = −55.5 (c = 0.47, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.11 (d, J = 7.2 Hz, 1H), 7.52−7.60 (m, 1H), 7.43 (d, J = 8.2 Hz, 2H), 7.35−7.37 (m,

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3H), 7.21−7.23 (m, 1H), 4.78−4.83 (m, 2H), 3.01−3.04 (m, 2H), 2.27−2.30 (m, 1H), 1.95−1.99 (m, 1H), 1.20 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −172.4 (dd, J = 23.0, 13.1 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.40 (d, J = 18.0 Hz), 142.4, 134.8, 134.7, 134.5, 131.1, 130.5, 129.0, 128.8, 128.6, 127.5, 94.9 (d, J_{CF} = 193.1 Hz), 58.10 (d, J = 19.5 Hz), 55.9, 31.0 (d, J = 21.8 Hz), 25.3 (d, J = 9.7 Hz), 22.6. IR (cm^{-1}): 2924, 1793, 1649, 1559, 1453, 1223, 1069, 906, 740. MS (ESI) m/z: 408.1 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{21}H_{24}ClFNO_2S^+$ $[M + H]^+$ 408.1195, found 408.1199

*(Rs)-N-[(R)-((S)-2-Fluoro-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)(furan-2-yl)methyl]-2-methylpropane-2-sulfinamide (**3ae**).* By following the general procedure, **3ae** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (151 mg, 83%), mp 104−106 °C; $[\alpha]_D^{20}$ = −98.5 (c = 0.58, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07−8.09 (m, 1H), 7.55 (td, J = 7.5, 1.3 Hz, 1H), 7.43 (d, J = 1.0 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.23−7.29 (m, 1H), 6.39−6.47 (m, 2H), 5.14 (dd, J = 19.5 (J_{HCCF}), 3.4 Hz, 1H), 4.43 (d, J = 2.8 Hz, 1H), 3.11−3.14 (m, 2H), 2.37−2.56 (m, 1H), 2.16−2.20 (m, 1H), 1.23 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −169.5 (td, J = 19.7, 10.9 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 192.5 (d, J = 18.2 Hz), 149.2, 142.8, 142.7, 134.6, 130.6, 128.9, 128.6, 127.3, 111.1, 110.7, 94.90 (d, J_{CF} = 191.6 Hz), 56.1, 54.0 (d, J = 21.6 Hz), 30.5 (d, J = 21.5 Hz), 25.3 (d, J = 8.9 Hz), 22.5. IR (cm^{-1}): 2960, 1610, 1364, 1469, 1278, 1175, 1011, 938, 742. MS (ESI) m/z: 364.1 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{19}H_{23}FNO_3S^+$ $[M + H]^+$ 364.1377, found 364.1374.

*(Rs)-N-[(R,E)-1-((S)-2-Fluoro-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)-3-phenylallyl]-2-methylpropane-2-sulfinamide (**3af**).* By following the general procedure, **3af** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a solid (152 mg, 76%), mp 142−143 °C; $[\alpha]_D^{20}$ = −11.4 (c = 0.54, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.09 (d, J = 7.8 Hz, 1H), 7.55 (t, J = 7.2 Hz, 1H), 7.44 (d, J = 7.3 Hz, 2H), 7.33 (m, 5H), 6.79 (d, J = 15.9 Hz, 1H), 6.16 (dd, J = 15.9, 9.0 Hz, 1H), 4.54−4.62 (m, 1H), 4.43 (s, 1H), 3.03−3.22 (m, 2H), 2.45−2.55 (m, 2H), 1.26 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −171.4 (*br*). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.00 (d, J = 18.1 Hz), 142.6, 136.4, 135.8, 134.6, 130.8, 128.9, 128.8, 128.7, 128.4, 127.4, 126.8, 123.2 (d, J = 3.2 Hz), 95.2 (d, J_{CF} = 190.5 Hz), 58.3 (d, J = 20.5 Hz), 56.0, 30.5 (d, J = 21.6 Hz), 25.1 (d, J = 9.3 Hz), 22.7. IR (cm^{-1}): 3279, 2952, 1691, 1450, 1303, 1229, 1100, 899, 742. MS (ESI) m/z: 400.2 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{23}H_{27}FNO_2S^+$ $[M + H]^+$ 400.1741, found 400.1746.

*(R)-N-[(R)-1-((R)-3-Fluoro-4-oxochroman-3-yl)butyl]-2-methylpropane-2-sulfinamide (**3bg**).* By following the general procedure, **3bg** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (125 mg, 73%), mp 114−116 °C; $[\alpha]_D^{20}$ = −129.1 (c = 0.53, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.88 (dd, J = 7.8, 1.5 Hz, 1H), 7.51−7.61 (m, 1H), 7.09 (dd, J = 12.0, 5.6 Hz, 2H), 5.22 (dd, J = 11.7, 4.4 Hz, 1H), 4.33 (dd, J = 11.7, 4.3 Hz, 1H), 3.71−3.91 (m, 2H), 1.35−1.75 (m, 4H), 1.30 (s, 9H), 0.82 (t, J = 7.3 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −189.1 (d, J = 23.6 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 189.7 (d, J = 16.7 Hz), 161.0, 136.9, 127.6, 122.3, 119.4, 118.2, 93.5 (d, J_{CF} = 191.9 Hz), 69.0 (d, J = 32.1 Hz), 57.2, 56.6 (d, J = 20.8 Hz), 29.7 (s), 22.9 (s), 19.2 (s), 13.6. IR (cm^{-1}): 2959, 1697, 1604, 1479, 1140, 1060, 912, 764. MS (ESI) m/z: 342.1 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{17}H_{25}FNO_3S^+$ $[M + H]^+$ 342.1534, found 342.1533.

*(Rs)-N-[(R)-1-((R)-3-Fluoro-4-oxochroman-3-yl)-3-methylbutyl]-2-methylpropane-2-sulfinamide (**3bh**).* By following the general procedure, **3bh** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (135 mg, 76%), mp 146−147 °C; $[\alpha]_D^{20}$ = −144.5 (c = 0.49, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.88 (dd, J = 8.0, 1.4 Hz, 1H), 7.47−7.63 (m, 1H), 7.03−7.18 (m, 2H), 5.28 (dd, J = 11.7, 4.5 Hz, 1H), 4.35 (dd, J = 11.7, 4.1 Hz, 1H), 3.73−3.93 (m, 2H), 1.63−1.80 (m, 2H), 1.30 (s, 9H), 1.11−1.20 (m, 1H), 0.88 (d, J = 6.6 Hz, 3H), 0.67 (d, J = 6.5 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −189.1 (d, J = 22.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 189.6 (d, J = 16.8 Hz), 160.9, 136.9, 127.5, 122.3, 118.8 (d, J = 129.0 Hz), 93.4 (d, J_{CF} = 192.0 Hz), 69.1 (d, J = 32.0 Hz), 57.3, 55.4 (d, J = 21.0 Hz), 39.5, 23.8 (d, J = 70.6 Hz), 22.9, 20.4. IR (cm^{-1}): 2955, 1697, 1470, 1335, 1319, 1219, 1099, 826, 762. MS (ESI) m/z: 356.2 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{18}H_{27}FNO_3S^+$ $[M + H]^+$ 356.1690, found 356.1699.

*(Rs)-N-[(R)-((S)-6-Fluoro-5-oxo-6,7,8,9-tetrahydro-5H-benzo[7]-annulen-6-yl)(p-tolyl)methyl]-2-methylpropane-2-sulfinamide (**3db**).* By following the general procedure, **3db** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a pale yellow liquid (160 mg, 80%); $[\alpha]_D^{20}$ = −42.0 (c = 0.49, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.61 (dd, J = 7.6, 0.9 Hz, 1H), 7.37−7.43 (m, 1H), 7.29−7.36 (m, 5H), 7.19 (d, J = 7.6 Hz, 1H), 5.00 (dd, J = 22.1 (J_{HCCF}), 6.2 Hz, 1H), 4.37 (d, J = 6.3 Hz, 1H), 3.14 (dd, J = 16.3, 10.4 Hz, 1H), 2.91 (dd, J = 16.4, 7.5 Hz, 1H), 2.05 (s, 3H), 1.63−1.82 (m, 2H), 1.27 (t, J = 7.1 Hz, 2H), 1.12 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −167.0 (*br*). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 203.8 (d, J = 30.1 Hz), 141.3, 137.3, 136.9, 131.5, 129.2, 129.1, 129.0, 128.4, 128.2, 126.6, 104.2 (d, J_{CF} = 190.9 Hz), 63.0 (d, J = 20.3 Hz), 56.0, 34.6 (d, J = 21.8 Hz), 33.5, 29.7, 23.5, 22.4. IR (cm^{-1}): 2930, 1693, 1601, 1451, 1364, 1234, 1069, 999, 837. MS (ESI) m/z: 402.2 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{23}H_{29}FNO_2S^+$ $[M + H]^+$ 402.1898, found 402.1895.

*(Rs)-N-[(1R,2S)-1-(4-Chlorophenyl)-2-fluoro-2-methyl-3-oxo-3-phenylpropyl]-2-methylpropane-2-sulfinamide (**3gd**).* By following the general procedure, **3gd** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a colorless liquid (163 mg, 83%); $[\alpha]_D^{20}$ = −78.0 (c = 0.46, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.86 (d, J = 7.8 Hz, 2H), 7.54 (t, J = 7.5 Hz, 1H), 7.40 (t, J = 7.8 Hz, 2H), 7.30 (s, 1H), 7.20−7.26 (m, 3H), 4.91 (dd, J = 17.5 (J_{HCCF}), 5.4 Hz, 1H), 4.50 (s, 1H), 1.63 (d, J_{HCCF} = 22.4 Hz, 3H), 1.13 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −160.4 (t, J = 22.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 201.7 (d, J = 25.7 Hz), 136.7, 135.3, 133.0, 129.3, 129.3, 129.1, 128.2, 128.1, 103.1 (d, J_{CF}= 193.6 Hz), 64.3 (d, J = 21.8 Hz), 56.2, 29.7, 22.4. IR (cm^{-1}): 2953, 1795, 1556, 1458, 1323, 1221, 1061, 812, 741. MS (ESI) m/z: 396.1 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{20}H_{24}FClNO_2S^+$ $[M + H]^+$ 396.1195, found 396.1192.

*(Rs)-N-[(1R,2S)-3-(Adamantan-1-yl)-2-fluoro-3-oxo-1-(p-tolyl)-propyl]-2-methylpropane-2-sulfinamide (**3hb**).* By following the general procedure, **3hb** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (155 mg, 74%), mp 142−143 °C; $[\alpha]_D^{20}$ = −45.8 (c = 0.53, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.19 (d, J = 7.7 Hz, 2H), 7.12 (d, J = 7.7 Hz, 2H), 5.26 (dd, J = 47.9 (J_{HCF}), 5.7 Hz, 1H), 4.82−4.93 (m, 1H), 4.37 (s, 1H), 2.31 (s, 3H), 1.93 (s, 3H), 1.56−1.78 (m, 12H), 1.20 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −187.8 (dd, J = 47.9, 15.7 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 204.0 (d, J = 16.0 Hz), 133.6, 128.1 (d, J = 3.5 Hz), 124.5, 123.9, 86.2 (d, J_{CF} = 189.9 Hz), 53.7 (d, J = 19.7 Hz), 51.1, 41.8, 31.7, 31.5, 22.7 (d, J = 11.1 Hz), 17.8 (d, J = 35.0 Hz), 16.4. IR (cm^{-1}):3190, 2911, 1704, 1505, 1454, 1361, 1050, 996, 845, 788. MS (ESI) m/z: 420.2 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{24}H_{35}FNO_2S^+$ $[M + H]^+$ 420.2367, found 420.2364.

*(Rs)-N-[(1R,2S)-3-((3S,5S,7S)-Adamantan-1-yl)-1-(4-bromophenyl)-2-fluoro-3-oxopropyl]-2-methylpropane-2-sulfinamide (**3hi**).* By following the general procedure, **3hi** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (195 mg, 81%), mp 116−118 °C; $[\alpha]_D^{20}$ = −43.8 (c = 0.71, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.45 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H), 5.27 (dd, J = 47.3 (J_{HCF}), 5.6 Hz, 1H), 4.79−4.91 (m, 1H), 4.48 (s, 1H), 1.95 (s, 3H), 1.49−1.77 (m, 12H), 1.20 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −188.6 (dd, J = 47.2, 16.4 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 208.9 (d, J = 16.4 Hz), 135.4, 131.7, 130.3, 122.6, 91.2 (d, J_{CF} = 191.4 Hz), 58.3 (d, J = 20.1 Hz), 56.0, 46.7, 36.5, 34.3, 27.4, 22.5. IR (cm^{-1}): 2908, 1707, 1588, 1488, 1364, 1233, 1037, 848, 816. MS (ESI) m/z: 484.1 $[M + H]^+$. HRMS (ESI) m/z: calcd for $C_{23}H_{32}BrFNO_2S^+$ $[M + H]^+$ 484.1316, found 484.1308.

*Methyl 4-[(1R,2S)-3-(Adamantan-1-yl)-1-((Rs)-1,1-dimethylethylsulfinamido)-2-fluoro-3-oxopropyl]benzoate (**3hj**).* By following the general procedure, **3hj** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a liquid (169 mg,

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73%), mp 94−95 °C; $[\alpha]_D^{20}$ = −41.5 (*c* = 0.58, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.90−8.10 (m, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 5.33 (dd, *J* = 47.2 (J_{HCF}), 5.5 Hz, 1H), 4.96 (dd, *J* = 11.4, 4.8 Hz, 1H), 4.53 (s, 1H), 3.89 (s, 3H), 1.94 (s, 3H), 1.49−1.87 (m, 12H), 1.21 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −188.2 (dd, *J* = 46.4, 16.4 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 204.2 (d, *J* = 16.7 Hz), 161.6 (d, *J* = 47.7 Hz), 136.7, 125.5, 125.0, 123.9, 86.6 (d, J_{CF} = 191.9 Hz), 56.4, 54.1 (d, *J* = 20.1 Hz), 51.3, 47.5, 42.0, 31.5 (d, *J* = 28.0 Hz), 22.6 (d, *J* = 11.0 Hz), 17.8 (d, *J* = 33.3 Hz). IR (cm^{-1}): 3433, 2959, 1700, 1604, 1463, 1313, 1140, 919, 799. MS (ESI) *m*/*z*: 464.2 $[M + H]^+$. HRMS (ESI) *m*/*z*: calcd for $C_{25}H_{35}FNO_4S^+$ $[M + H]^+$ 464.2265, found 464.2262.

*(Rs)-N-[(1R,2S)-3-((3S,5S,7S)-Adamantan-1-yl)-2-fluoro-1-(4-nitrophenyl)-3-oxopropyl]-2-methylpropane-2-sulfinamide (**3hk**).* By following the general procedure, **3hk** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (200 mg, 89%), mp 148−149 °C; $[\alpha]_D^{20}$ = −43.1 (*c* = 0.51, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.21 (d, *J* = 8.7 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2H), 5.38 (dd, *J* = 46.6 (J_{HCF}), 5.0 Hz, 1H), 5.01 (dt, *J* = 17.0, 4.9 Hz, 1H), 4.71 (d, *J* = 3.9 Hz, 1H), 1.98 (s, 3H), 1.60−1.68 (m, 12H), 1.25 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −189.3 (dd, *J* = 46.4, 16.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 209.3 (d, *J* = 17.0 Hz), 147.9, 144.2, 129.5, 123.7, 91.1 (d, J_{CF} = 193.2 Hz), 58.7 (d, *J* = 20.6 Hz), 56.3, 46.9, 36.6, 36.2, 27.4, 22.5. IR (cm^{-1}): 3391, 2914, 1704, 1521, 1451, 1348, 1105, 1044, 702. MS (ESI) *m*/*z*: 451.2 $[M + H]^+$. HRMS (ESI) *m*/*z*: calcd for $C_{23}H_{32}FN_2O_4S^+$ $[M + H]^+$ 451.2061, found 451.2055.

*(Rs)-N-[(1R,2S)-3-((3S,5S,7S)-Adamantan-1-yl)-1-(4-cyanophenyl)-2-fluoro-3-oxopropyl]-2-methylpropane-2-sulfinamide (**3hl**).* By following the general procedure, **3hl** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (174 mg, 81%), mp 141−142 °C; $[\alpha]_D^{20}$ = −50.6 (c = 0.54, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.63 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H), 5.34 (dd, *J* = 46.7 (J_{HCF}), 5.0 Hz, 1H), 4.93 (dt, *J* = 16.9, 4.9 Hz, 1H), 4.63 (d, *J* = 3.5 Hz, 1H), 1.96 (s, 3H), 1.52−1.74 (m, 12H), 1.22 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −189.2 (dd, *J* = 46.4, 16.0 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 209.3 (d, *J* = 16.6 Hz), 142.1, 132.2, 129.3, 118.4, 112.4, 91.7 (d, J_{CF} = 193.6 Hz), 58.8 (d, *J* = 20.4 Hz), 56.2, 46.9, 36.5, 36.2, 27.4, 22.5. IR (cm^{-1}): 2904, 2222, 1720, 1383, 1047, 1024, 993, 839, 755, 735. MS (ESI) *m*/*z*: 431.2 $[M + H]^+$. HRMS (ESI) *m*/*z*: calcd for $C_{24}H_{32}FN_2O_2S^+$ $[M + H]^+$ 431.2163, found 431.2156.

*(Rs)-N-[(1R,2S)-1-(4-Bromophenyl)-2-fluoro-3-(2-methoxyphenyl)-3-oxopropyl]-2-methylpropane-2-sulfinamide (**3ji**).* By following the general procedure, **3ji** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a colorless liquid (171 mg, 75%); $[\alpha]_D^{20}$ = −53.4 (*c* = 0.56, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.74 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.44−7.58 (m, 3H), 7.23−7.36 (m, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 8.7 Hz, 1H), 5.99 (dt, *J* = 47.6 (J_{HCF}), 5.6 Hz, 1H), 4.92 (dt, *J* = 21.7 (J_{HCCF}), 3.6 Hz, 1H), 4.35 (d, *J* = 3.5 Hz, 1H), 3.92 (d, *J* = 5.5 Hz, 3H), 1.21 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −198.9 (dd, *J* = 47.8, 21.8 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 195.9 (d, *J* = 19.2 Hz), 158.4, 137.0, 135.1, 131.6, 131.5, 129.8, 124.8, 122.3, 121.4, 111.4, 95.3 (d, J_{CF} = 190.3 Hz), 57.9 (d, *J* = 19.1 Hz), 56.0, 55.7, 22.5. IR (cm^{-1}): 2953, 1701, 1601, 1435, 1287, 1175, 1018, 890, 761. MS (ESI) *m*/*z*: 456.1 $[M + H]^+$. HRMS (ESI) *m*/*z*: calcd for $C_{20}H_{24}FBrNO_3S^+$ $[M + H]^+$ 456.0639, found 456.0639.

*(Rs)-N-[(1R,2S)-2-Fluoro-4,4-dimethyl-3-oxo-1-phenylpentyl]-2-methylpropane-2-sulfinamide (**3na**).* By following the general procedure, **3na** was isolated by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1) as a white solid (114 mg, 70%), mp 90−91 °C; $[\alpha]_D^{20}$ = −63.2 (*c* = 0.38, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.28 (m, 5H), 5.33 (dd, *J* = 47.4 (J_{HCF}), 5.9 Hz, 1H), 4.95 (dt, *J* = 15.0, 5.3 Hz, 1H), 4.60 (s, 1H), 1.24 (s, 9H), 0.92 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −185.6 (dd, *J* = 47.2, 15.2 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 210.5 (d, *J* = 17.4 Hz), 136.2, 128.6, 128.5, 92.6 (d, J_{CF} = 192.0 Hz), 59.4 (d, *J* = 20.3 Hz), 56.0, 44.4, 24.9 (d, *J* = 1.6 Hz), 22.6. IR (cm^{-1}): 2972, 1716, 1683, 1513, 1501, 1457, 1338, 1046, 893, 704. MS (ESI) *m*/*z*: 328.2 $[M + H]^+$. HRMS (ESI) *m*/*z*: calcd for $C_{17}H_{27}FNO_2S^+$ $[M + H]^+$ 328.1741, found 328.1743.

Procedure for the Synthesis of *tert*-Butyl (1*R*,2*S*)-3-(Adamantan-1-yl)-1-(4-bromophenyl)-2-fluoro-3-oxopropyl) Carbamate (4). Compound **3hi** (483 mg, 1 mmol) was dissolved in 3 mL of methanol, followed by the addition of 4 N HCl/MeOH (1 mL). The reaction mixture was stirred at rt for 30 min and was then concentrated to dryness. A solution of $(Boc)_2O$ (240 mg, 1.1 mmol) and NEt_3 (0.3 mL, 2.2 mmol) in THF (3 mL) was added to the obtained intermediate, and the mixture was stirred at rt for 6 h. Concentration of the reaction mixture under vacuum, followed by flash column chromatography (petroleum ether/ethyl acetate = 10/1), afforded product **4** as a white solid (436 mg, 91%), mp 109−110 °C; $[\alpha]_D^{20}$ = −9.6 (*c* = 0.28, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.50 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 5.52 (s, 1H), 5.22−5.39 (m, 2H), 2.06 (s, 3H), 1.92 (d, *J* = 11.9 Hz, 3H), 1.70−1.93 (m, 12H), 1.42 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ = −199.2 (dd, *J* = 46.6, 27.2 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 208.7 (d, *J* = 17.2 Hz), 154.8, 137.6, 131.8, 128.7, 121.9, 93.9 (d, J_{CF} = 191.6 Hz), 80.3, 54.5, 46.5, 37.2, 36.3, 28.2, 27.7. IR (cm^{-1}): 2914, 1759, 1486, 1364, 1246, 1159, 1072, 1002, 778. MS (ESI) *m*/*z*: 480.2 $[M + H]^+$. HRMS (ESI) *m*/*z*: calcd for $C_{24}H_{32}BrFNO_3^+$ $[M + H]^+$ 480.1544, found 480.1542.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01979.

X-ray crystal structure of compound **3ad** (CIF)
X-ray crystal structure of compound **3na** (CIF)
X-ray crystal structure of compound **3aa′** (CIF)
Copies of ^1H, ^{19}F, and ^{13}C NMR spectra of all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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