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Asymmetric Allylation/RCM-Mediated Synthesis of Fluorinated Benzo-Fused Bicyclic Homoallylic Amines As Dihydronaphthalene Derivatives

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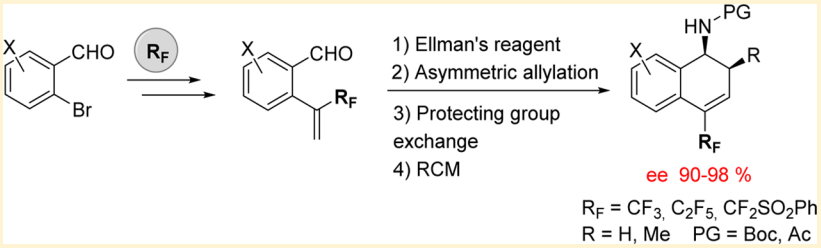
Supporting Information



ABSTRACT: Enantiomerically enriched fluorinated benzo-fused bicyclic homoallylic amines have been synthesized through an asymmetric allylation/ring closing metathesis (RCM) sequence. This sequence has been carried out using α-trifluoromethylstyrene derivatives as key intermediates, synthesized by microwave radiation. The great deactivating effect exerted by such substituents has been brought to light by a comparative study.

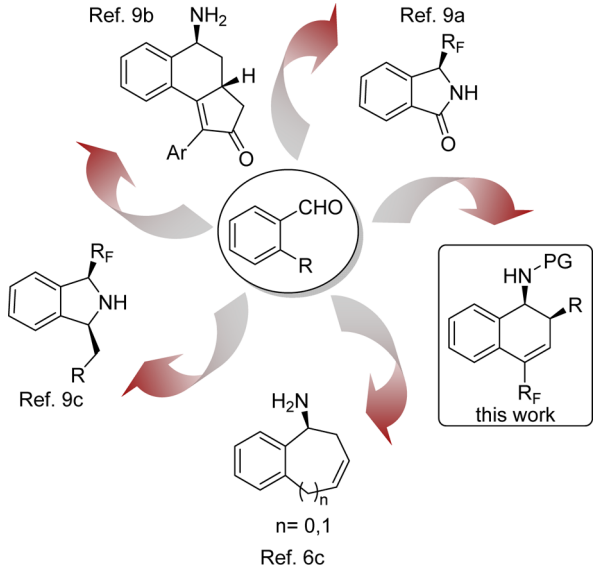
INTRODUCTION

In recent years, the importance of organofluorine compounds in pharmacy and agrochemistry has dramatically increased,[1] due to the beneficial effects brought about by the incorporation of fluorine or fluorine-containing groups in organic molecules, such as increased metabolic stability or lipophilicity.[2] For this reason, the interest in the development of new methodologies for the introduction of fluorinated units in organic molecules has rapidly increased.

In this context, chiral homoallylic amines are interesting building blocks in organic synthesis, and one of the most important methods for their preparation is the asymmetric allylation of imines.[3] Specifically, the diastereoselective addition of allylzinc bromide to Ellman's *tert*-butylsulfinyl imines represents the most advantageous method with a high degree of diastereocontrol and chemical yields, reliability, and functional group compatibility.[4] This methodology has recently been combined with the ring closing metathesis reaction (RCM), one of the most versatile methods for the construction of medium-sized rings,[5] for the synthesis of cyclic amino acid derivatives, pyrazolopyridines, pyrazoloazepines[6a] and, more recently, benzo-fused systems.[6b,c]

Therefore, continuing our work within the context of diversity oriented synthesis (DOS)[7,8] focused on the use of *tert*-butylsulfinyl imines derived from *ortho*-substituted benzaldehydes,[9,10] a small library of fluoroalkylated 1-amino-1,2-hydronaphthalene derivatives is described herein (Scheme 1). It is worth mentioning that such derivatives are unprecedented in the literature.

Scheme 1. Diversity Oriented Synthesis Strategy



Dihydronaphthalene, as a bicyclic molecular scaffold, has been used as model for the design of many interesting pharmacophores.[11] Some noteworthy examples include sertraline (Figure 1a), a selective serotonin reuptake inhibiting (SSR1) antidepressant,[5,12] or podophyllotoxin (Figure 1b),

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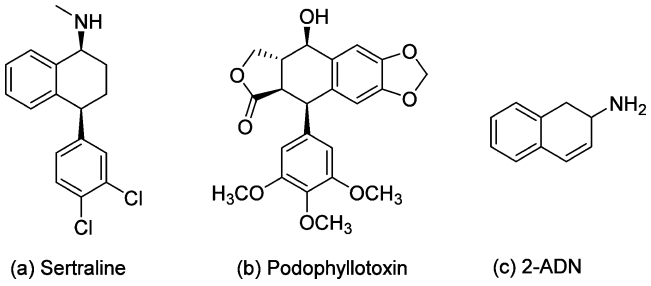


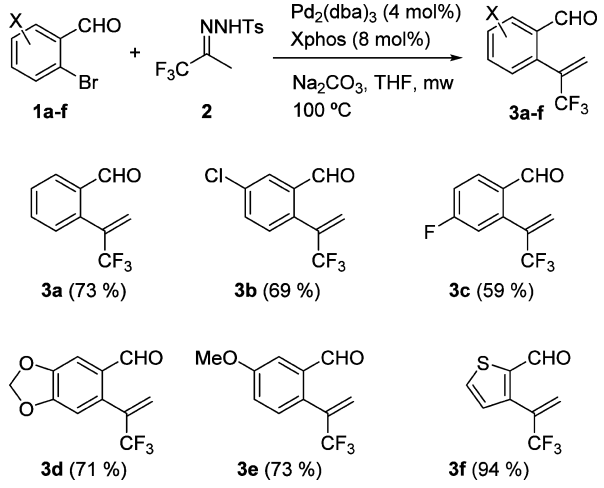
Figure 1. Examples of natural products containing the hydronaphthalene substructure.

which has a wide range of medical applications in purgative, vesicant, antirheumatic, antiviral, and antitumor agents.[13] 2-ADN (Figure 1c), also a 1,2-dihydronaphthalene derivative, represents a new, potent and conformationally restricted analog of amphetamine.[14] It produces stimulation of spontaneous motor activity in mice, and the racemate is approximately one-fourth as potent as (+)-amphetamine on a molar basis.

RESULTS AND DISCUSSION

In view of this background, and given our interest in fluorinated compounds, we describe a practical method for the synthesis of various fluorinated benzo-fused homoallylic amines (Scheme 1, this work) using *fluorinated building blocks* **3** as key intermediates (Scheme 2). The strategy described by Valdés

Scheme 2. Synthesis of α-Trifluoromethylstyrenes 3a−f



et al. for the synthesis of α-trifluoromethylstyrenes is a highly versatile technique permitting the addition of fluorinated single-carbon units.[15] This method proceeds through a Palladium-catalyzed cross coupling reaction of 1,1,1-trifluoromethylacetone tosylhydrazone **2** with aryl bromides **1** and represents an alternative to the coupling between boronic acids and 2-bromo-3,3,3-trifluoropropene.[16] However, the original reaction conditions failed when applied to our model substrate 2-bromobenzaldehyde **1a**. A small optimization allowed the determination of the best reaction conditions for complete conversion, which for our system involved microwave heating at 100 °C and an increase in palladium catalytic loading with respect to the conditions already described, finally affording products **3a−f** in good yields. These compounds were used immediately after their purification in the next reaction step due to their instability.

With aldehyde intermediates **3a−f** in hand, and based on our recent research,[6,9] the strategy next required the synthesis of the corresponding Ellman's (*R*)-*N*-(*tert*-butanesulfinyl)imines **4a−f** followed by the allylation reaction, giving rise to products **5a−f** in moderate to good yields and excellent diastereoselectivities (Scheme 3).[17] The obtained results show that electron-donating (**3d**,**e**), halogen substituents (**3b**,**c**), and heteroaromatic imines (**3f**) are all compatible with the reactions conditions. Moreover, the crotylation reaction made the formation of a new stereocenter possible, and compound **5g** was obtained in 82% yield as a single diastereoisomer (Scheme 3).

According to our synthetic strategy, and once a varied library of substrates had been obtained, we set out to apply the RCM reaction as a suitable approach to synthesize the corresponding fluorinated dihydronaphthalene derivatives. Unfortunately, despite several attempts under different reaction conditions, the outcome was not satisfactory for the RCM of **5a**, most likely due to the presence of the *tert*-butanesulfinyl group and the lower reactivity of fluorinated olefins in metathesis processes.[18] In view of this result, we next evaluated the influence of the *N*-protecting group.[6c] To this end, *N*-Boc and *N*-Ac protected amines **6a−g**, **6a′** and **6f′** were prepared and subjected to the RCM reaction in the presence of 5 mol % of second Generation Grubbs catalyst [Ru-**II**] in toluene at 100 °C, leading to the bicyclic derivatives **7a−g**, **7a′** and **7f′** (Scheme 4).

In view of the good results obtained with α-CF_3-substituted 2-vinylbenzaldehyde derivatives, we decided to extend our methodology to other α-fluoroalkylated 2-vinylbenzaldehyde systems. In addition, we envisioned the preparation of two nonfluorinated α-substituted 2-vinylbenzaldehyde derivatives in order to study the influence of fluoroalkyl groups directly attached to a vinyl moiety on their reactivity in olefin metathesis reactions. However, the strategy described above (see Scheme 2) proved inefficient for the synthesis of other fluoroalkylated substrates by the cross-coupling reaction of tosylhydrazones containing different R_F (C_2F_5, CF_2H, CF_2SO_2Ph and $CFHSO_2Ph$). Therefore, alternative synthetic sequences were set up for each substrate (Scheme 5). The corresponding CH_3- and C_2F_5-substituted substrates **3h**,**i** were prepared by means of palladium-catalyzed Suzuki cross-coupling reactions (Scheme 5, eq 1). It is worth noting that, regarding fluoroalkylated substrates, this methodology has mainly been studied for the trifluoromethyl group and to a much lesser extent for other fluorinated groupings.[16b] On the other hand, substrates bearing electron-withdrawing groups at the α-position of the styrene, such as the ester or difluorosulfone,[19] were synthesized by a Wittig methylenation of the corresponding ketones **13a**,**b** (Scheme 5, eq 2). Final deprotection of the *ortho* acetal group yielded the desired substrates **3j**,**k**.

Next, the condensation and allylation steps proceeded uneventfully affording substrates **5h−k** in moderate to good yields with good to complete diastereoselectivities (Scheme 6). Due to their lack of reactivity (vide infra), fluoroalkylated sulfinamides **5h**,**k** were converted into the corresponding *tert*-butyl carbamate **6h** or acetamide **6k**, respectively (Scheme 6).

The final RCM step revealed the dramatic effect of the fluoroalkyl substituent at the vinyl group on its performance in olefin metathesis processes (Scheme 7).[18] More specifically, although this step proceeded in high yields with sulfinamides **5i**,**j** at room temperature using the Hoveyda−Grubbs second

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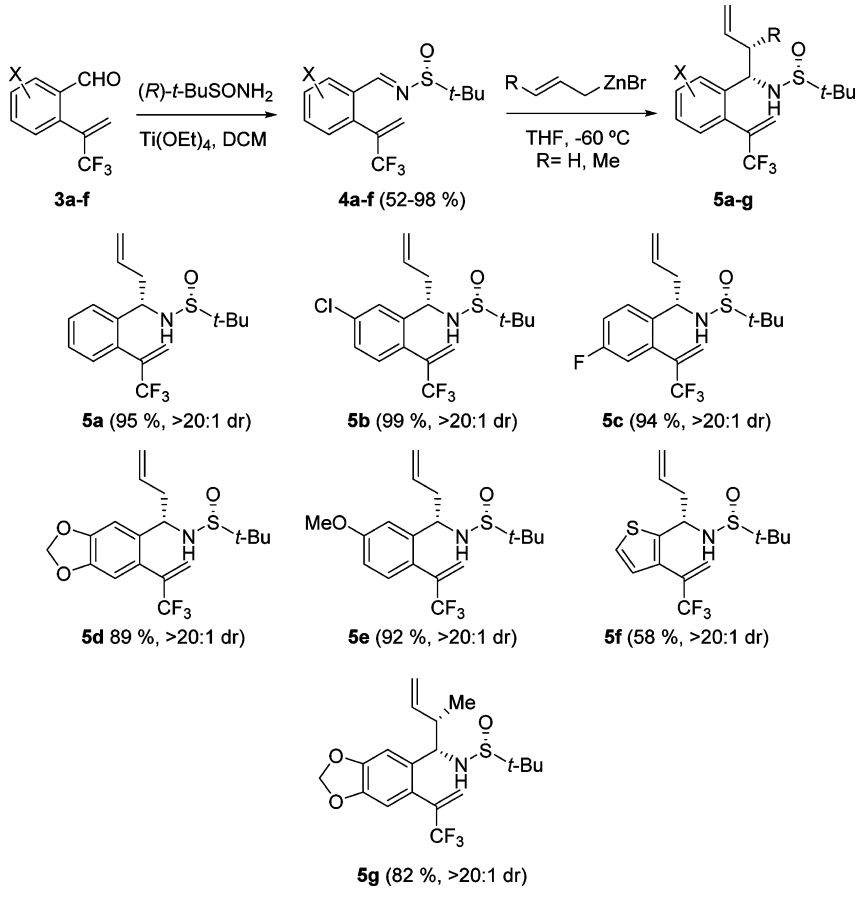
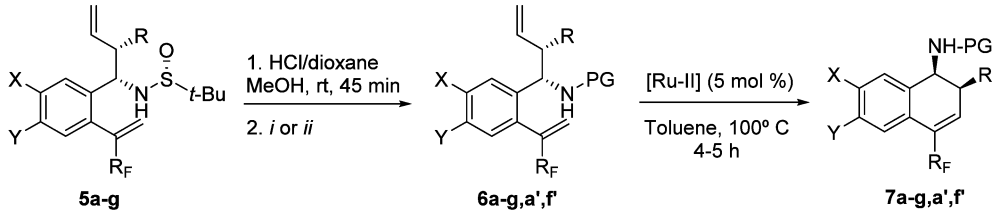
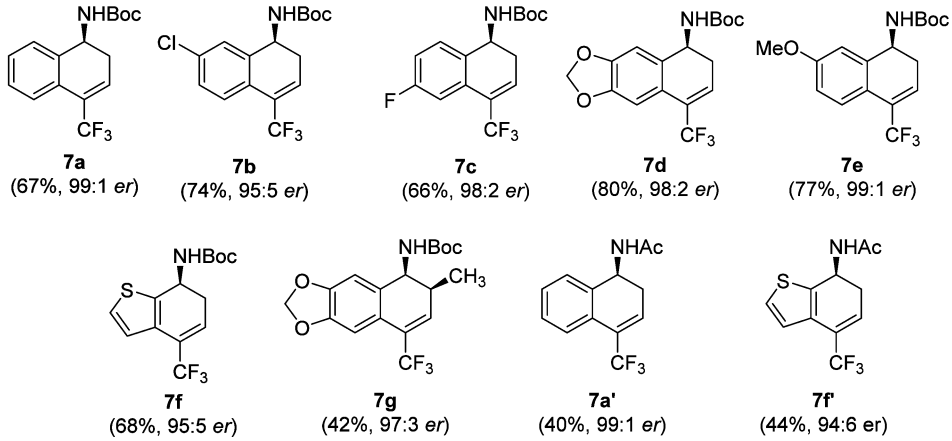
Scheme 3. Asymmetric Allylation of Sulfinimines 4a−h



Scheme 4. Protecting Group Exchange and RCM



Reaction conditions: (*i*) Boc_2O (1.3 equiv), K_2CO_3 (2.5 equiv), 50 °C, 1,4-dioxane, 20 h; (*ii*) Ac_2O (1.5 equiv), Et_3N (2 equiv), DMAP (0.02 equiv), 0 °C, CH_2Cl_2, 16 h



generation catalyst [Ru-**III**] in DCM, fluoroalkylated substrates **5h**,**k** required a protecting group exchange to either Boc or Ac in order to participate in the RCM step using [Ru-**II**] or [Ru-**III**], respectively (Scheme 7). Moreover, the reaction temper-

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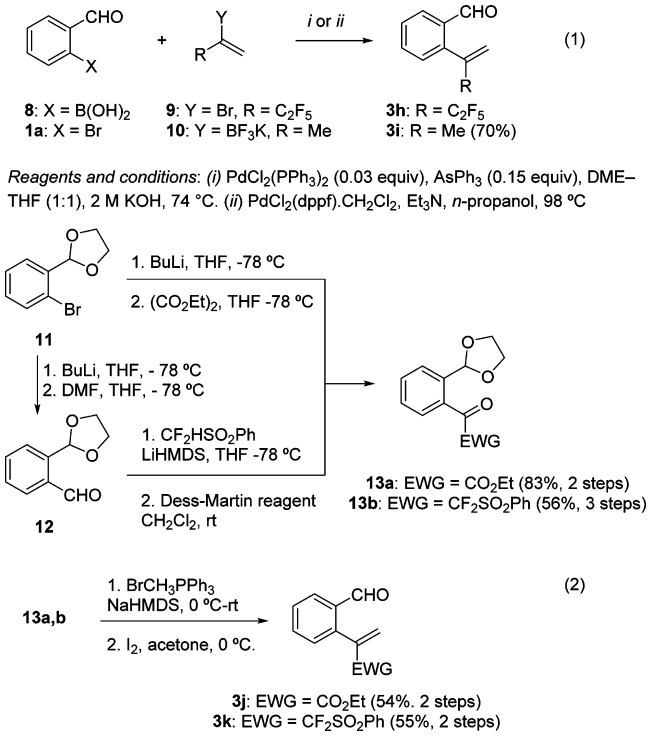
Scheme 5. Synthesis of Substrates 3h−k



ature had to be increased to 100 °C in toluene, showcasing the deactivating effect of fluoroalkyl substituents directly attached to vinyl group in olefin metathesis reactions (Scheme 7). It should be noted that, not only the CH_3-substituted substrate **5i** but also the acrylate derivative **5j** reacted at room temperature, indicating that the deactivating effect of a fluoroalkyl group is higher than that of an ester group. Besides this noticeable deactivating effect of fluoroalkyl groups, we have also observed a trend in the influence of the several protecting groups used: may only be used for the nonfluorine containing substituents while any fluoroalkyl substitution requires the use of an acetyl or a carbamate protecting groups. This may indicate that the *tert*-butylsulfinyl group is somewhat deactivating for homoallylic amines in metathesis processes.

CONCLUSION

In summary, a new approach to the synthesis of 1-amino-4-fluoroalkyl-1,2-dihydronaphthalene derivatives from readily available *ortho*-fluoroalkylvinyl benzaldehydes has been developed, with a particular emphasis on those bearing trifluoromethyl substituents. Additionally, we have studied the deactivating effect of such fluoroalkyl substitution on RCM reactions. We can conclude that α-fluoroalkylated styrenes are much less reactive than the corresponding nonfluorinated α-substituted ones. This deactivation is much more pronounced than for common electron-withdrawing groups, i.e., esters. Building on the principles of diversity-oriented synthesis, a new family of fluorinated building-blocks suitable for the preparation of more complex molecules has been described. Further applications for the, in our opinion, understudied α-CF_3-substituted 2-vinylbenzaldehyde scaffold are currently underway in our laboratories.

EXPERIMENTAL SECTION

General Methods. Reactions were carried out under a nitrogen atmosphere unless otherwise indicated. Solvents were purified prior to use: THF and PhMe were distilled from sodium and CH_2Cl_2 from calcium hydride. The reactions were monitored with the aid of TLC on 0.25 mm precoated silica-gel plates. Visualization was carried out with UV light and aqueous ceric ammonium molybdate solution or potassium permanganate stain. Flash column chromatography was performed with the indicated solvents on silica gel 60 (particle size: 0.040−0.063 mm). ^1H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer. Chemical shifts are given in ppm (δ), referenced to the residual proton resonances of the solvents. Coupling constants (J) are given in Hertz (Hz). The letters m, s, d, t, and q stand for multiplet, singlet, doublet, triplet, and quartet, respectively. The letters br indicate that the signal is broad. The abbreviations DCM and THF indicate dichloromethane and tetrahydrofuran.

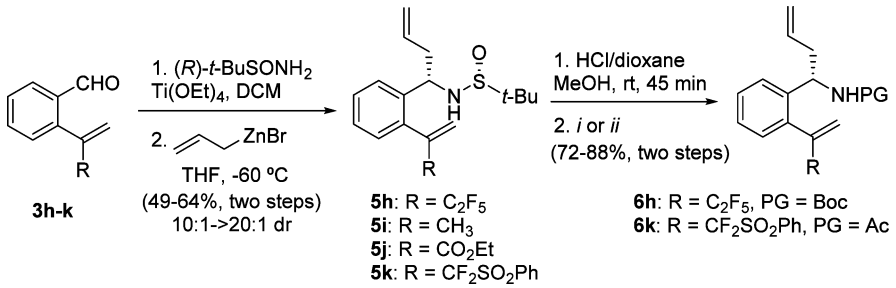
Microwave reactions were carried out in a 2−5 or 15 mL vial with a Biotage InitiatorTM 2.0 microwave synthesizer. The solutions were stirred before the irradiation was started and the absorbance of the solvent was set as "normal". The reaction time was initiated as soon the system reached the input temperature, although it took approximately 2 min to reach it.

QTOF mass analyzer system has been used for the HRMS measurements.

Enantiomeric excess was determined by means of HPLC using a chiral columns and mixtures of hexane and isopropanol as mobile phase.

Synthesis of 3a−f. *General Procedure.* A 5 mL microwave glass vial was charged with $Pd_2(dba)_3$ (4 mol %, 0.07 mmol), Xphos (8 mol %, 0.09 mmol), Na_2CO_3 (2.2 equiv, 2.37 mmol) and *N*-tosylhydrazone **2** (1.40 mmol, 1.3 equiv), which was previously prepared from 1,1,1−trifluoroacetone (1 equiv, 22 mmol) and tosylhydrazide (1 equiv, 22 mmol) by heating at 70 °C in EtOH (0.5 M) for 5 h and then filtering the precipitate solid at room temperature as a crystalline white solid. The solid reagents were dried together under reduced pressure before being used. THF (0.3 M) and the corresponding *o*-bromobenzaldehyde **1** (1.08 mmol) were added. The vial was sealed and the mixture was heated by microwave irradiation at 100 °C for 1.5 h. The reaction

Scheme 6. Condensation/Asymmetric Allylation/Protecting Group Exchange Sequence[a]



[a]Reaction conditions: (i) Boc_2O (1.3 equiv), K_2CO_3 (2.5 equiv), 50 °C, 1,4-dioxane, 20 h; (ii) Ac_2O (1.5 equiv), Et_3N (2 equiv), DMAP (0.02 equiv), 0 °C, CH_2Cl_2, 16 h.

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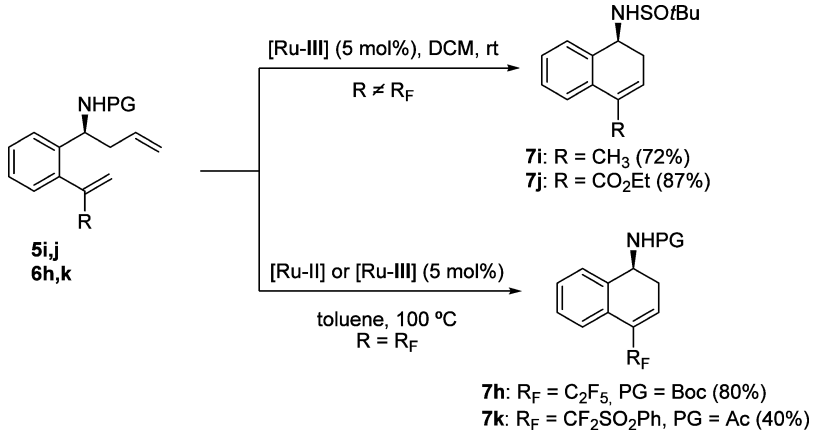
Scheme 7. RCM on Fluorinated and Nonfluorinated α-Substituted 2-Vinylbenzaldehyde Derivatives



mixture was cooled to room temperature, opened, filtered through Celite and concentrated under reduced pressure. The residue obtained was purified by flash chromatography and used immediately for the next condensation reaction.[20]

*2-(3,3,3-Trifluoro-1-propen-2-yl)benzaldehyde (**3a**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (30:1)] afforded **3a** as a yellow oil (73%, 200 mg). The spectroscopic data of **3a** are consistent with those described in the literature.[21]

*5-Chloro-2-(3,3,3-trifluoro-1-propen-2-yl)benzaldehyde (**3b**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (30:1)] afforded **3b** as a yellow oil (69%, 250 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.64 (q, J = 3.0 Hz, 1H), 6.32 (q, J = 3.0 Hz, 1H), 7.36 (dd, J = 3.0, 1.5 Hz, 1H), 7.59 (dd, J = 8.4, 2.4 Hz, 1H), 7.97 (d, J = 3.0 Hz, 1H), 10.07 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 122.3 (q, J^1_{CF} = 273.9 Hz; CF_3), 125.6 (q, J^3_{CF} = 4.7 Hz; C), 128.2 (CH), 132.1 (CH), 133.6 (CH), 134.4 (q, J^3_{CF} = 30.2 Hz; C), 134.4 (q, J^3_{CF} = 30.2 Hz; C), 134.7 (C), 136.0 (C), 136.3 (C), 189.4 (CHO) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.5 (s, 3F; CF_3) ppm.

*4-Fluoro-2-(3,3,3-trifluoro-1-propen-2-yl)benzaldehyde (**3c**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (30:1)] afforded **3c** as a colorless oil (59%, 220 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.67 (q, J = 2.7 Hz, 1H), 6.32 (q, J = 3.0 Hz, 1H), 7.12 (dd, J = 8.7, 2.4 Hz, 1H), 7.28−7.21 (m, 2H), 8.05 (dd, J = 8.7, 5.7 Hz, 1H), 10.05 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 117.1 (d, J^2_{CF} = 21.7 Hz; CH), 117.8 (d, J^2_{CF} = 23.0 Hz; CH), 122.1 (q, J^1_{CF} = 273.8 Hz; CF_3), 125.7 (q, J^3_{CF} = 4.8 Hz; C), 131.2 (d, J^3_{CF} = 9.9 Hz; CH), 131.5 (d, J^3_{CF} = 2.8 Hz; CH), 134.4 (q, J^2_{CF} = 32.5 Hz; C), 139.1 (d, J^3_{CF} = 9.4 Hz; CH), 165.2 (d, J^1_{CF} = 264.2 Hz; CF), 189.0 (CHO) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −103.2 to −103.1 (m, 1F; CF), −66.4 (s, 3F; CF_3) ppm.

*6-(3,3,3-Trifluoro-1-propen-2-yl)benzo[d][1,3]dioxole-5-carbaldehyde (**3d**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (20:1)] afforded **3d** as a yellow solid (71%, 200 mg). mp 74−76 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.74 (q, J = 1.2 Hz, 1H), 5.22 (s, 2H), 5.41 (q, J = 1.5 Hz, 1H), 5.94 (s, 1H), 6.56 (s, 1H), 9.06 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 102.4 (CH2), 106.7 (CH), 110.6 (CH), 125.3 (q, J^1_{CF} = 273.8 Hz; CF3), 125.7 (q, J^3_{CF} = 4.8 Hz; C), 130.4 (C), 133.5 (C), 134.6 (q, J^2_{CF} = 31.9 Hz; CH_2), 149.0 (C), 152.1 (C), 189.0 (CHO) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.6 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{11}H_7F_3O_3$ [M + H^+]: 245.0420, found 245.0416.

*5-Methoxy-2-(3,3,3-trifluoro-1-propen-2-yl)benzaldehyde (**3e**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (20:1)] afforded **3e** as a yellow oil (73%, 300 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.88 (s, 3H), 5.58 (q, J = 1.2 Hz, 1H), 6.37 (q, J = 1.5 Hz, 1H), 7.16 (dd, J = 8.7, 3.0 Hz, 1H), 7.32 (d, J = 8.7 Hz, 1H), 7.48 (d, J = 3.0 Hz, 1H), 10.08 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 55.6 (CH_3), 111.0 (CH), 120.9 (CH), 122.5 (q, J^1_{CF} = 273.9 Hz; CF_3), 125.3 (q, J^3_{CF} = 4.8 Hz; CH_2), 129.3 (CH), 131.9 (CH), 134.9 (q, J^2= 32.1 Hz; C), 136.1 (C), 160.3 (C), 190.7 (CHO) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.6 (s, 3F; CF_3) ppm.

*3-(3,3,3-Trifluoro-1-propen-2-yl)thiophene-2-carbaldehyde (**3f**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (20:1)] afforded **3f** as a yellow oil (94%, 500 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.74 (q, J = 1.5 Hz, 1H), 6.27 (q, J = 1.5 Hz, 1H), 7.16−7.19 (m, 1H), 7.72 (dd, J = 4.8, 1.2 Hz, 1H), 9.85 (d, J = 1.5 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 122.1 (q, J^1_{CF} = 273.8 Hz; CF_3), 126.1 (q, J^3_{CF} = 5.1 Hz; CH_2), 129.5 (C), 131.9 (q, J^2_{CF} = 32.5 Hz; C), 134.1 (C), 141.4 (C), 142.2 (C), 182.9 (CHO) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.0 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_8H_5F_3OS$ [M + H^+]: 207.0086, found 207.0081.

Synthesis of 3h. To a solution of **9** (1.3 equiv, 0.87 mmol) in DME−THF (1:1, 2 mL) and aq. Two M KOH (1.3 mL), the phenylboronic acid **8** (1 equiv, 0.67 mmol), $PdCl_2(PPh_3)_2$ (0.03 equiv, 0.02 mmol), and $AsPh_3$ (0.15 equiv; 0.1 mmol) were added under an inert atmosphere in a sealed tube. The mixture was stirred at 74 °C for 12 h. The mixture was cooled to room temperature, H_2O (5 mL) was added, and the mixture was extracted with Et_2O (2 × 10 mL). The combined organic layers were washed with brine and dried ($MgSO_4$). The solvent was removed and the crude residue was used immediately in the next condensation reaction.

Synthesis of 3i. A solution of potassium isopropenyltrifluoroborate **10** (237 mg, 1.6 mmol), $PdCl_2$(dppf).CH_2Cl_2 (21 mg, 0.03 mmol), *o*-bromobenzaldehyde **1a** (237 mg, 1.28 mmol), and Et_3N (0.2 mL, 1.4 mmol) in *n*-PrOH (20 mL) was heated at 98 °C under a N_2 atmosphere for 13 h. Then the mixture was cooled to room temperature, and diluted with water (10 mL) followed by extraction with diethyl ether (20 mL). The ethereal layer was washed with brine (10 mL) and dried over $MgSO_4$. The solvent was removed in vacuo, and the crude product was purified by silica gel chromatography (eluting with hexane/DCM 30:1) affording 2-(1-propen-2-yl)-benzaldehyde (130 mg, 0.9 mmol, 70%), whose spectroscopic data are consistent with those described in the literature.[22] This product was used immediately for the next condensation reaction.

Synthetic Strategy for the Synthesis of 3j. Synthesis of ketone **13a**: *n*-BuLi (2.5 M in *n*-hexane, 1.24 mmol, 0.5 mL) was added slowly to a solution of 2-bromobenzaldehyde ethylene acetal **11** (1.12 mmol, 0.2 mL) in THF (10 mL) at −78 °C. After stirring for 1h, diethyloxalate (1.24 mmol, 0.17 mL) was added to the mixture at −78 °C. The mixture was stirred for 3h, and at this time, saturated aqueous NH_4Cl was added. The mixture was extracted with Et_2O and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under vacuum. The residue was purified by flash chromatography [*n*-hexane: Et_2O (7:1)] to afford **13a** (188 mg, 70%). whose spectroscopic data are consistent with those described in the literature.[23]

Wittig methylenation: NaHMDS (1 M in toluene, 1.4 mL, 0.822 mmol) was added dropwise to a suspension of methyl triphenylphosphonium chloride (294 mg, 0.822 mmol) in THF (4 mL) at 0 °C under nitrogen atmosphere. The resulting mixture was stirred at this temperature for 45 min, after which a solution of **13a** (525 mg, 0.685 mmol) in THF (4 mL) was slowly added. The reaction mixture was

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stirred at room temperature until **13a** was no longer detectable by TLC (12 h). The reaction mixture was then hydrolyzed with a saturated solution of NH_4Cl (3 mL) and extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo to give a yellow oil, which was purified by means of column chromatography on silica gel [*n*-hexane-EtOAc (10:1)] to afford ethyl 2-[2-(1,3-dioxolan-2-yl)phenyl]acrylate (Wittig product **I**) as a colorless oil (60%, 120 mg). ^{1}H NMR (CD_3OD, 300 MHz) δ 1.24 (t, J = 7.2 Hz, 3H), 3.91−3.93 (m, 2H), 4.00−4.03 (m, 2H), 4.19 (q, J = 7.2, 2H), 5.70 (d, J = 2.0 Hz, 1H), 5.71 (s, 1H), 6.45 (d, J = 2.0 Hz, 1H), 7.15−7.18 (m, 1H), 7.35−7.38 (m, 2H), 7.53−7.56 (m, 1H) ppm. ^{13}C NMR (CD_3OD, 75.5 MHz) δ 14.5 (CH_3), 62.2 (CH_2), 64.4 ($2CH_2$), 102.9 (CH), 127.7 (CH), 128.1 (CH_2), 128.9 (CH), 129.4 (CH), 131.4 (CH), 137.4 (*C*), 138.0 (*C*), 143.1 (*C*), 168.2 (*C*) ppm. HRMS (EI) calcd. for $C_{14}H_{16}O_4$ [M + H^+]: 249.1121, found 249.1114.

Acetal group deprotection: to a solution of the Wittig product (420 mg, 1.15 mmol) in acetone (6 mL) at 0 °C, I_2 (one bead) was added and the mixture was stirred at this temperature for 5 h. After this time, the solvent was removed under reduced pressure and the residue was purified by flash chromatography [*n*-hexane-EtOAc (7:1)] affording **3j** as a colorless oil (54% two steps, 150 mg), whose spectroscopic data are consistent with those described in the literature.[24]

Synthetic Strategy for the Synthesis of 3k. CF_2HSO_2Ph addition: In a round-bottom flask, 2-bromobenzaldehyde ethylene acetal **11** (5 mmol, 1 equiv) was dissolved in dry THF (25 mL) and cooled to −78 °C. Then a solution of *n*-BuLi (2.6 M in hexane, 7.5 mmol, 1.5 equiv) was added dropwise and stirred for 1 h at the same temperature. Then, *N*,*N*-dimethylformamide (7.5 mmol, 1.5 equiv) was added dropwise and the reaction mixture was allowed to warm up to 0 °C. The reaction was quenched with a saturated solution of ammonium chloride and the mixture was extracted with diethyl ether. The organic phase was subsequently washed with brine and dried over anhydrous sodium sulfate. The solvent was evaporated in vacuo, and crude **12** (883 mg, 4.96 mmol) was dissolved in THF (24 mL). $PhSO_2CF_2H$ (0.9 mL, 5.95 mmol) was added, and the mixture was cooled at −78 °C. At this temperature, LiHMDS (1 M in THF, 6.5 mL, 6.5 mmol) was added dropwise and the mixture was stirred for 15 h. Saturated aq. NH_4Cl was then added at −78 °C and the residue was brought to room temperature and extracted with diethyl ether. The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. Flash chromatography of the crude reaction mixture [*n*-hexane-EtOAc (4:1)] afforded 1-[2-(1,3-dioxolan-2-yl)phenyl]-2,2-difluoro-2-(phenylsulfonyl)-1-ethanol (*addition product* ***II***) as a colorless oil (70%, 1.2 g). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.63 (br, 1H), 4.00−4.07 (m, 2H), 4.12−4.20 (m, 2H), 5.95 (s, 1H), 6.22 (d, J = 22.5 Hz, 1H), 7.35−7.42 (m, 2H), 7.55−7.62 (m, 3H), 7.71−7.76 (m, 2H), 8.02 (d, J = 7.5 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 65.1 (CH_2), 65.2 (CH_2), 66.2 (dd, J^2_{CF} = 27.2, 18.4; CH), 102.1 (CH), 120.7 (dd, J^1_{CF} = 299.9, 289.4; CF_2), 126.9 (CH), 128.8 (CH), 128.9 (CH), 129.2 (CH), 129.5 (CH), 130.7 (CH), 132.9 (C), 139.0 (C), 135.4 (CH), 135.8 (C) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −119.1 (ddd, J = 238.3, 22.6, 1.9 Hz; 1F; C*F*F), −103.0 (d, J = 238.3 Hz, 1F; CF*F*). HRMS (EI) calcd. for $C_{17}H_{20}F_2NO_5S$ [M + NH_4^+]: 388.1025, found 388.1025.

Oxidation to ketone **13b**: To a solution of the alcohol obtained in the previous step (626 mg, 1.69 mmol) in DCM (17 mL), $NaHCO_3$ (20 mg) and Dess−Martin periodinane were added (907 mg, 2.03 mmol) at room temperature. The reaction mixture was stirred at room temperature for 2 h and was then filtered through Celite and the filtrate was extracted with H_2O and saturated aq. $NaHCO_3$. The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography using as eluent hexane:EtOAc (4:1) to afford 1-[2-(1,3-dioxolan-2-yl)phenyl]-2,2-difluoro-2-(phenylsulfonyl)-1-ethanone **13b** as a colorless oil (80%, 520 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.74−3.82 (m, 2H), 3.85−3.93 (m, 2H), 6.12 (s, 1H), 7.50−7.55 (m, 3H), 7.60−7.69 (m, 3H), 7.76−7.81 (m, 1H), 7.99−8.02 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 64.5 ($2CH_2$), 101.5 (CH), 114.7 (t, J^1_{CF} = 303.4; CF_2), 126.9 (CH), 127.9 (CH), 129.0 (CH), 129.3 (2CH), 130.9 (2CH), 131.5 (CH), 132.8 (*C*), 133.1 (*C*), 135.8 (CH), 138.6 (*C*), 190.2 (t, J^2_{CF} = 25.2; CO) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −105.5 (s, 2F; CF_2) ppm. HRMS (EI) calcd. for $C_{17}H_{18}F_2O_5SN$ [M + NH_4^+]: 386.0874, found 386.0870.

Wittig reaction and acetal deprotection: The Wittig reaction to afford 2-{2-[3,3-difluoro-3-(phenylsulfonyl)-1-propen-2-yl]phenyl}-1,3-dioxolane and deprotection of the acetal group to afford **3k**, were carried out following the methodology described in the previous section. Flash chromatography [*n*-hexane-EtOAc (6:1)] afforded 2-{2-[3,3-difluoro-3-(phenylsulfonyl)-1-propen-2-yl]phenyl}-1,3-dioxolane (Wittig product ***III***), as a colorless oil (78%, 235 mg). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.97−4.16 (m, 4H), 5.88 (s, 1H), 5.96 (t, J = 0.9 Hz, 1H), 6.37 (t, J = 1.5 Hz, 1H), 7.37−7.46 (m, 3H), 7.55−7.60 (m, 2H), 7.65−7.75 (m, 2H), 7.97 (d, J = 7.20 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 65.4 ($2CH_2$), 101.5 (CH), 120.4 (t, J^1_{CF} = 288.3; CF_2), 126.8 (CH), 128.7 (CH), 128.9 (CH), 129.1 (2CH), 129.95 (t, J^3_{CF} = 6.8; CH_2), 130.3 (CH), 130.8 (2CH), 132.9 (*C*), 133.8 (*C*), 134.6 (t, J^2_{CF} = 22.1; *C*), 135.1 (CH), 136.7 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −97.7 (br, 2F; CF_2) ppm. HRMS (EI) calcd. for $C_{18}H_{20}F_2O_4SN$ [M + NH_4^+]: 384.1081, found 384.1076. Deprotection of the acetal group and flash chromatography purification [*n*-hexane-EtOAc (7:1)] afforded 2-[3,3-difluoro-3-(phenylsulfonyl)-1-propen-2-yl]benzaldehyde **3k** as a white solid (70%, 260 mg). mp 120−122 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.91 (t, J= 0.9 Hz, 1H), 6.42 (t, J= 1.5 Hz, 1H), 7.54−7.60 (m, 5H), 7.72−7.78 (m, 1H), 7.94−7.99 (m, 3H), 10.18 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 120.1 (t, J^1_{CF} = 288.9; CF_2), 129.1 (CH), 129.3 (2CH), 129.4 (CH), 130.2 (t, J^3_{CF} = 6.8; CH_2), 130.8 (2CH), 131.7 (CH), 132.6 (*C*), 133.5 (CH), 134.4 (t, J^2_{CF} = 22.3; *C*), 135.0 (*C*), 135.4 (CH), 136.9 (*C*), 191.3 (CHO) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −99.3 (s, 2F; CF_2) ppm. HRMS (EI) calcd. for $C_{16}H_{16}F_2O_3SN$ [M + NH_4^+]: 340.0819, found 340.0814.

General Procedure for the Condensation of Aldehydes ***3*** *to Imines* ***4***. A solution of the corresponding aldehyde **3** (5 mmol, 1.0 equiv) and $Ti(OEt)_4$ (5.0 equiv) in dichloromethane (0.1 M) was stirred for 5 min at room temperature. To the resulting solution, (*R*)-*N*-(*tert*-butanesulfinyl)amine was added, and the mixture was stirred at room temperature for 12 h. After this time, saturated aqueous $NaHCO_3$ was added until white titanium salts precipitated. The suspension was filtered through a short pad of Celite washing with small portions of dichloromethane. The filtrate was extracted with ethyl acetate and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under vacuum. The residue was purified by flash chromatography affording imines **4**.

(R_S*-E)-2-Methyl-N-[2-(3,3,3-trifluoro-1-propen-2-yl)benzylidene]-propane-2-sulfinamide (****4a****).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (5:1)] afforded **4a** as a yellow oil (95%, 525 mg). $[\alpha]_D^{25}$ = −13.9 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25 (s, 9H), 5.56 (q, J = 1.2 Hz, 1H), 6.25 (q, J = 1.5 Hz, 1H), 7.36−7.39 (m, 1H), 7.50−7.53 (m, 2H), 8.10−8.13 (m, 1H), 8.71 (s, 1H), ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.6 ($3CH_3$), 57.9 (*C*), 122.5 (q, CF_3, J^1_{CF} = 274.3), 124.9 (q, CH_2, J^3_{CF} = 5.0), 128.4 (CH), 129.3 (CH), 130.5 (CH), 131.6 (CH), 132.9 (*C*), 135.6 (*C*), 135.9 (q, *C*, J^2_{CF} = 31.7), 160.8 (CH) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.3 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{14}H_{17}F_3NOS$ [M + H^+]: 304.0977, found 304.0982.

(R_S*-E)-N-[5-Chloro-2-(3,3,3-trifluoro-1-propen-2-yl)benzylidene]-2-methylpropane-2-sulfinamide (****4b****).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (5:1)] afforded **4b** as a pale yellow solid (99%, 400 mg). $[\alpha]_D^{25}$ = −85.1 (*c* 1.0; $CHCl_3$). mp 49−51 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25 (s, 9H), 5.57 (q, J = 3.0 Hz, 1H), 6.28 (q, J = 3.0 Hz, 1H), 7.33 (d, J = 9.0 Hz, 1H), 7.48 (dd, J = 8.4, 2.4 Hz, 1H), 8.08 (d, J = 3.0 Hz, 1H), 8.63 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.6 ($3CH_3$), 58.2 (*C*), 122.3 (q, CF_3, J^1_{CF} = 271.8), 125.7 (q, CH_2, J^3_{CF} = 4.0), 125.7 (*C*), 128.1 (CH), 131.6 (CH), 131.8 (CH), 133.7 (*C*), 134.4 (*C*), 135.8 (*C*), 134.9 (q, *C*, J^2_{CF} = 31.9), 159.6 (CH) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.4 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{14}H_{16}F_3NOSCl$ [M + H^+]: 338.0588, found 338.0582.

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*(R_S-E)-N-[4-Fluoro-2-(3,3,3-trifluoro-1-propen-2-yl)benzylidene]-2-methylpropane-2-sulfinamide (**4c**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (5:1)] afforded **4c** as a white solid (94%, 425 mg). $[\alpha]_D^{25}$ = −116.94 (*c* 1.0; $CHCl_3$). mp 46−48 °C. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.24 (s, 9H), 5.60 (q, *J* = 1.20 Hz, 1H), 6.29 (q, *J* = 1.5 Hz, 1H), 7.09 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.18−7.25 (m, 1H), 8.14 (dd, *J* = 9.0, 6.0 Hz, 1H), 8.64 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.4 ($3CH_3$), 57.8 (*C*), 117.0 (d, *CH*, J^2_{CF} = 21.7), 117.8 (d, *CH*, J^2_{CF} = 20.7), 122.2 (q, CF_3, J^1_{CF} = 273.8), 125.6 (q, CH_2, J^3_{CF} = 5.1), 129.4 (q, *C*, J^3_{CF} = 5.0), 131.3 (d, *CH*, J^2_{CF} = 9.9), 131.5 (d, *CH*, J^3_{CF} = 2.8), 134.6 (q, *C*, J^2_{CF} = 31.9), 137.6 (d, *C*, J^3_{CF} = 8.9), 159.5 (*CH*), 164.1 (d, *CF*, J^1_{CF} = 256.7) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.3 (s, 3F; CF_3), −106.7 (s, 1F; *CF*) ppm. HRMS (EI) calcd. for $C_{14}H_{15}F_4NOS$ [M + H^+]: 322.0883, found 322.0875.

*(R_S-E)-2-Methyl-N-{[6-(3,3,3-trifluoro-1-propen-2-yl)benzo[d]-[1,3]dioxol-5-yl] methylene}propane-2-sulfinamide (**4d**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (5:1)] afforded **4d** as a white solid (89%, 300 mg). $[\alpha]_D^{25}$ = −50.3 (*c* 1.0; $CHCl_3$). mp 58−60 °C. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.23 (s, 9H), 5.55 (q, *J* = 1.5 Hz, 1H), 6.07 (d, *J* = 1.2 Hz, 1H), 6.08 (d, *J* = 1.2 Hz, 1H), 6.25 (q, *J* = 1.2 Hz, 1H), 6.81 (s, 1H), 7.58 (s, 1H), 8.57 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.5 ($3CH_3$), 57.7 (*C*), 102.1 (CH_2), 107.0 (*CH*), 109.7 (*CH*), 122.4 (q, CF_3, J^1_{CF} = 274.0), 125.5 (q, CH_2 J^3_{CF} = 4.7), 128.0 (*C*), 131.4 (*C*), 134.9 (q, *C*, J^2_{CF} = 31.5), 148.8 (*C*), 150.6 (*C*), 159.8 (*CHO*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.4 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{15}H_{17}F_3NO_3S$ [M + H^+]: 348.0876, found 348.0876.

*(R_S-E)-N-[5-Methoxy-2-(3,3,3-trifluoro-1-propen-2-yl)-benzylidene]-2-methylpropane-2-sulfinamide (**4e**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (5:1)] afforded **4e** as a colorless oil (92%, 350 mg). $[\alpha]_D^{25}$ = −80.1 (*c* 1.0; $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.21 (s, 9H), 3.83 (s, 3H), 5.48 (d, *J* = 1.5 Hz, 1H), 6.19 (d, *J* = 1.5 Hz, 1H), 7.02 (dd, *J* = 8.4, 2.7 Hz, 1H), 7.26 (d, *J* = 8.7 Hz, 1H), 7.58 (d, *J* = 2.7 Hz, 1H), 8.64 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.4 ($3CH_3$), 55.3 (OCH_3), 57.8 (*C*), 112.0 (*CH*), 118.1 (*CH*), 122.5 (q, CF_3, J^1_{CF} = 274.0), 120.7 (*C*), 125.0 (q, CH_2, J^3_{CF} = 4.7), 131.5 (*CH*), 134.0 (*C*), 134.0 (q, *C*, J^2_{CF} = 31.5), 135.4 (q, *C*, J^2_{CF} = 31.5), 159.5 (*C*), 160.0 (*C*), 160.7 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.0 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{15}H_{19}F_3NO_2S$ [M + H^+]: 334.1108, found 334.1093.

*(R_S-E)-2-Methyl-N-{[5-(3,3,3-trifluoro-1-propen-2-yl)benzo[b]-thiophen-6-yl]methylene}propane-2-sulfinamide (**4f**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (5:1)] afforded **4f** as a yellow oil (58%, 315 mg). $[\alpha]_D^{25}$ = −55.0 (*c* 1.0; $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.24 (s, 9H), 5.64 (q, *J* = 1.5 Hz, 1H), 6.22 (q, *J* = 1.5 Hz, 1H), 7.13−7.16 (m, 1H), 7.55 (dd, *J* = 5.4, 1.2 Hz, 1H), 8.63 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.5 ($3CH_3$), 58.2 (*C*), 120.4 (*C*), 125.7 (q, CH_2, J^3_{CF}= 5.05), 129.1 (*CH*), 131.4 (*CH*), 131.9 (q, *C*, J^2_{CF} = 32.16), 138.5 (*C*), 139.2 (*C*), 154.2 (*CH*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −66.9 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{12}H_{15}F_3NOS_2$ [M + H^+]: 310.0542, found 310.0545.

*(R_S-E)-2-Methyl-N-[2-(3,3,4,4,4-pentafluoro-1-buten-2-yl)-benzylidene]propane-2-sulfinamide (**4h**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (5:1)] afforded **4h** as colorless oil (66%, 100 mg). $[\alpha]_D^{25}$ = −60.2 (*c* 1.0; $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.23 (s, 9H), 5.71 (br, 1H), 6.28 (br, 1H), 7.30−7.33 (m, 1H), 7.47−7.50 (m, 2H), 8.09−8.12 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.5 ($3CH_3$), 57.8 (*C*), 113.1 (tq, J^1_{CF} = 255.4, J^2_{CF} = 38.1; CF_2F_3), 119.1 (qt, J^1_{CF} = 286.9, J^2_{CF} = 38.1; CF_2CF_3), 127.9 (t, J^3_{CF} = 7.6; CH_2), 128.4 (*CH*), 129.3 (*CH*), 130.8 (*CH*), 131.5 (*CH*), 132.9 (*C*), 135.4 (t, J^2_{CF} = 23.1; *C*), 139.9 (*C*), 160.8 (*CH*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −114.4 (q, *J* = 57.8 Hz, 2F; CF_2), −83.0 (t, *J* = 2.0 Hz, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{15}H_{17}F_5NOS$ [M + H^+]: 354.0946, found 354.0948.

*(R_S-E)-N-[2-(3,3-Difluoro-3-phenylsulfonyl-1-propen-2-yl)-benzylidene]-2-methylpropane-2-sulfinamide (**4k**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (5:1)] afforded **4k** as colorless oil (52%, 120 mg). $[\alpha]_D^{25}$ = −16.3 (*c* 1.0; $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.21 (s, 9H), 5.86 (t, *J* = 0.9 Hz, 1H), 6.32 (t, *J* = 1.5 Hz, 1H), 7.47−7.61 (m, 5H), 7.70−7.76 (m, 1H), 7.95−8.06 (m, 3H), 8.71 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.5 ($3CH_3$), 57.8 (*C*), 120.18 (t, J^1_{CF} = 289.1; CF_2), 128.7 (*CH*), 129.2 (2*CH*), 129.3 (*CH*), 129.9 (t, J^3_{CF} = 6.7; CH_2), 130.8 (2*CH*), 131.7 (2*CH*), 132.7 (*C*), 133.0 (*C*), 135.2 (t, J^2_{CF} = 22.3; *C*), 135.3 (*CH*), 136.1 (*C*), 161.3 (*CH*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −99.8 (br, 1F; *CF*F), −98.3 (br, 1F; CF*F*) ppm. HRMS (EI) calcd. For $C_{20}H_{22}F_2NO_3S_2$ [M + H^+]: 426.1005, found 426.1000.

*General Procedure for the Allylation/Crotylation of Imines **4**.* A 1 M solution of allylzinc/crotylzinc bromide in THF was prepared by stirring, allyl/crotyl bromide (1.0 equiv) and activated Zn (3.0 equiv) in anhydrous THF (1 M) at 55 °C. This freshly prepared solution (1.1 equiv, 0.55 mmol) was then added to a solution of imine **4** (1.0 equiv, 0.5 mmol) in THF (0.1 M) at −60 °C. After stirring for 3h at −60 °C the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted three times with AcOEt. Flash chromatography afforded compounds **5**.

*(R_S)-2-Methyl-N-{(S)-1-[2-(3,3,3-trifluoro-1-propen-2-yl)phenyl]-3-buten-1-yl} propane-2-sulfinamide (**5a**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (5:1)] afforded **5a** as colorless oil (95%, 250 mg). $[\alpha]_D^{25}$ = −225.8 (*c* 1.0; $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.09 (s, 9H), 2.24−2.50 (m, 2H), 3.69 (br, 1H), 4.54−4.59 (m, 1H), 5.10−5.16 (m, 2H), 5.66 (d, *J* = 3.0 Hz, 1H), 5.62−5.76 (m, 1H), 6.14 (q, *J* = 3.0 Hz, 1H), 7.17−7.22 (m, 2H), 7.33−7.41 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.6 ($3CH_3$), 43.1 (CH_2), 52.4 (*CH*), 55.6 (*C*), 119.4 (CH_2), 122.8 (q, CF_3, J^1_{CF} = 271.8), 124.2 (q, *CH*$_2$, J^3_{CF} = 4.9), 127.2 (*CH*), 127.7 (*CH*), 129.1 (*CH*), 129.9 (*CH*), 133.3 (*C*), 134.5 (*CH*), 136.6 (q, *C*, J^2_{CF} = 31.1), 140.8 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.5 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{17}H_{22}F_3NOS$ [M + H^+]: 346.1447, found 346.1437.

*(R_S)-N-{(S)-1-[5-Chloro-2-(3,3,3-trifluoro-1-propen-2-yl)phenyl]-3-buten-1-yl}-2-methylpropane-2-sulfinamide (**5b**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (5:1)] afforded **5b** as colorless oil (99%, 230 mg). $[\alpha]_D^{25}$ = −57.5 (*c* 1.0; $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.18 (s, 9H), 2.27−2.36 (m, 1H), 2.49−2.57(m, 1H), 3.76 (s, 1H), 4.60 (ddd, *J* = 6.0, 3.0, 0.5 Hz, 1H), 5.19−5.25 (m, 2H), 5.68−5.81 (m, 2H), 6.23 (dd, *J* = 3.0, 3.0 Hz, 1H), 7.18 (d, *J* = 9.0 Hz, 1H), 7.26−7.29 (m, 1H), 7.45 (d, *J* = 3.0 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.5 ($3CH_3$), 42.9 (CH_2), 52.2 (*CH*), 55.8 (*C*), 119.8 (CH_2), 122.5 (q, CF_3, J^1_{CF} = 203.8), 124.8 (q, CH_2, J^3_{CF} = 4.8), 127.5 (*CH*), 128.1 (*CH*), 131.3 (*CH*), 131.6 (*C*), 133.9 (*CH*), 135.7 (q, *C*, J^2_{CF} = 31.5), 142.9 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.5 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{17}H_{22}ClF_3NOS$ [M + H^+]: 380.1057, found 380.1053.

*(R_S)-N-{(S)-1-[4-Fluoro-2-(3,3,3-trifluoro-1-propen-2-yl)phenyl]-3-buten-1-yl}-2-methylpropane-2-sulfinamide (**5c**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (4:1)] afforded **5c** as colorless oil (94%, 265 mg). $[\alpha]_D^{25}$ = −103.4 (*c* 1.0; $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.15 (s, 9H; $3CH_3$), 2.27−2.38 (m, 1H), 2.46−2.52 (m, 1H), 3.75 (s, 1H), 4.57 (ddd, *J* = 5.7, 3.9, 1.5 Hz, 1H), 5.16−5.21 (m, 2H), 5.66−5.80 (m, 2H), 6.22 (q, *J* = 1.2 Hz, 1H), 6.93 (dd, *J* = 9.3, 2.7 Hz, 1H), 7.09 (dt, *J* = 8.4, 3.0 Hz, 1H), 7.43 (dd, *J* = 5.7, 2.2 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.5 ($3CH_3$), 43.1 (CH_2), 51.8 (*CH*), 55.6 (*C*), 116.4 (d, *CH*, J^2_{CF} = 10.1), 116.7 (d, *CH*, J^2_{CF} = 11.0), 119.5 (CH_2), 122.6 (q, CF_3, J^1_{CF} = 273.6), 124.7 (q, CH_2, J^3_{CF} = 4.8), 129.7 (q, *CH*, J^3_{CF} = 8.4), 134.16 (*CH*), 135.0 (d, *C*, J^3_{CF} = 8.0), 135.4 (q, *C*, J^2_{CF} = 31.3), 136.6 (d, *C*, J^3_{CF} = 3.1), 161.1 (d, *CF*, J^1_{CF} = 249.1) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −114.8 (ddd, J_{FH}= 9.0, 8.2, 5.6 Hz, F; *CF*), −67.5 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{17}H_{22}F_4NOS$ [M + H^+]: 364.1353, found 364.1345.

*(R_S)-2-Methyl-N-{(S)-1-[6-(3,3,3-trifluoro-1-propen-2-yl)benzo[d]-[1,3]dioxol-5-yl]-3-buten-1-yl}propane-2-sulfinamide (**5d**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (4:1)] afforded **5d** as colorless oil (89%, 225 mg). $[\alpha]_D^{25}$ = −61.6 (*c* 1.0; $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.17 (s, 9H), 2.24−2.38 (m, 1H), 2.44−2.51 (m, 3H), 3.72 (s, 1H), 4.54 (ddd, *J* = 9.6, 3.9, 1.5 Hz, 1H), 5.15−5.21 (m, 2H), 5.67−5.77 (m, 2H), 5.98 (dd, *J* = 6.0, 1.2 Hz, 2H), 6.18 (q, *J* = 1.2 Hz, 1H), 6.67 (s, 1H), 6.88 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.5 ($3CH_3$), 43.1 (CH_2), 52.3 (*CH*),

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55.5 (*C*), 101.4 (CH_2), 107.2 (*CH*), 109.4 (*CH*), 119.3 (CH_2), 122.8 (q, CF_3, J^1_{CF} = 273.3), 124.6 (q, CH_2, J^3_{CF} = 4.6), 134.4 (*C*), 134.6 (*CH*), 135.0 (q, *C*, J^2_{CF} = 31.2), 136.6 (*C*), 145.6 (*C*), 148.5 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.6 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{18}H_{23}F_3NO_3S$ [M + H^+]: 390.1345, found 390.1356.

*(R_S)-N-{(S)-1-[5-Methoxy-2-(3,3,3-trifluoro-1-propen-2-yl)phenyl]-3-buten-1-yl}-2-methylpropane-2-sulfinamide (**5e**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (4:1)] afforded **5e** as a white solid (92%, 280 mg). $[\alpha]_D^{25}$ = −91.7 (*c* 1.0; $CHCl_3$). mp 60−62 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (s, 9H), 2.28−2.40 (m, 1H), 2.50−2.57 (m, 1H), 3.73 (br, 1H), 3.81 (s, 3H), 4.60 (ddd, *J* = 9.6, 3.9, 1.8 Hz, 1H), 5.17−5.23 (m, 2H), 5.69 (q, *J* = 1.5 Hz, 1H), 5.71−5.83 (m, 1H), 6.19 (q, *J* = 1.2 Hz, 1H), 6.84 (dd, *J* = 8.4, 2.7 Hz, 1H), 6.98 (d, *J* = 2.7 Hz, 1H), 7.16 (d, *J* = 9.0 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.5 ($3CH_3$), 43.1 (*CH*), 52.5 (CH_2), 55.1 (OCH_3), 55.6 (*C*), 112.9 (*CH*), 112.8 (*CH*), 119.4 (CH_2), 122.9 (q, CF_3, J^1_{CF} = 273.8 Hz), 124.4 (q, CH_2, J^3_{CF} = 4.0 Hz), 125.5 (*C*), 131.1 (*CH*), 134.4 (*CH*), 135.9 (q, *C*, J^2_{CF} = 31.1 Hz), 142.4 (*C*), 160.0 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.7 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{18}H_{25}F_3NO_2S$ [M + H^+]: 376.1553, found 376.1560.

*(R_S)-2-Methyl-N-{(S)-1-[5-(3,3,3-trifluoro-1-propen-2-yl)benzo[b]thiophen-6-yl]-3-buten-1-yl}propane-2-sulfinamide (**5f**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (4:1)] afforded **5f** as colorless oil (58%, 450 mg). $[\alpha]_D^{25}$ = −75.7(*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.20 (s, 9H), 2.42−2.53 (m, 1H), 2.57−2.64 (m, 1H), 3.79 (s, 1H), 4.78−4.83 (m, 1H),), 5.16−5.22 (m, 2H), 5.78−5.80 (m, 1H), 5.64−5.77 (m, 1H), 6.12 (q, *J* = 1.5 Hz, 1H), 6.93 (dd, *J* = 5.4, 1.2 Hz, 1H), 7.28 (d, *J* = 4.8 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.9 ($3CH_3$), 44.9 (CH_2), 50.9 (*CH*), 55.8 (*C*), 117.2 (*C*), 119.8 (*C*), 120.2 (CH_2), 124.3 (q, J^3_{CF}= 5.13 Hz, CH_2), 125.2 (*CH*), 128.2 (*CH*), 132.5 (q, J^2_{CF}= 31.63 Hz; *C*), 133.9 (*CH*), 145.2 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.3 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{15}H_{20}F_3NOS_2$ [M + H^+]: 352.1011, found 352.1008.

*(R_S)-2-Methyl-N-{(1S,2S)-2-methyl-1-[6-(3,3,3-trifluoro-1-propen-2-yl)benzo[d][1,3]dioxol-5-yl]-3-buten-1-yl}propane-2-sulfinamide (**5g**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (3:1)] afforded **5g** as colorless oil (82%, 133 mg). $[\alpha]_D^{25}$ = −71.1 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.75 (d, *J* = 6.9 Hz, 3H), 1.15 (s, 9H), 2.28−2.41 (m, 1H), 3.98 (s, 1H), 4.21 (dd, *J* = 9.3, 0.9 Hz, 1H), 5.17−5.25 (m, 2H), 5.63−5.75 (m, 1H), 5.93 (d, *J* = 1.2 Hz, 1H), 5.99 (dd, *J* = 4.5, 1.5 Hz, 2H), 6.21 (q, *J* = 1.5 Hz, 1H), 6.72 (d, *J* = 0.9 Hz, 1H), 6.82 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 16.9(CH_3), 22.6 ($3CH_3$), 47.5 (*CH*), 55.6 (*C*), 56.4 (*CH*), 101.5 (CH_2), 107.4 (*CH*), 108.9 (*CH*), 117.7 (CH_2), 121.1 (q, J^1_{CF} = 273.3 Hz; CF_3), 124.6 (*C*), 125.6 (q, J^3_{CF}= 4.9 Hz; CH_2), 132.9 (*C*), 135.6 (q, J^2_{CF}= 30.7 Hz; *C*), 146.7 (*C*), 141.6 (*CH*), 148.5 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −65.5 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{19}H_{24}F_3NO_3S$ [M + H^+]: 404.1502, found 404.1523.

*(R_S)-2-Methyl-N-{(S)-1-[2-(3,3,4,4,4-pentafluoro-1-buten-2-yl)-phenyl]-3-buten-1-yl}propane-2-sulfinamide (**5h**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (5:1)] afforded **5h** as a white solid (91%, 180 mg). $[\alpha]_D^{25}$ = −90.2 (*c* 1.0; $CHCl_3$). mp 59−61 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.15 (s, 9H), 2.32−2.40 (m, 1H), 2.51−2.58 (m, 1H), 3.78 (br, 1H), 4.56−4.61 (m, 1H), 5.17−5.24 (m, 2H), 5.50−5.83 (m, 1H), 5.88 (s, 1H), 6.23 (s, 1H), 7.17−7.19 (m, 1H), 7.24−7.30 (m, 1H), 7.36−7.47 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.5 ($3CH_3$), 42.9 (CH_2), 52.6 (*CH*), 55.6 (*C*), 108.8−125.0 (C_2F_5), 119.4 (CH_2), 127.1 (*CH*), 127.6 (t, J^3_{CF} = 7.7, CH_2), 127.7 (*CH*), 129.1 (*CH*), 130.1 (*CH*), 133.8 (*C*), 134.5 (*CH*), 140.9 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −112.8 (d, *J* = 181.3 Hz, 2F; CF_2), −82.7 (s, 3; CF_3) ppm. HRMS (EI) calcd. for $C_{18}H_{22}F_5OSN$ [M + H^+]: 396.1415, found 396.1422.

*(R_S)-2-Methyl-N-{(S)-1-[2-(1-propen-2-yl)phenyl]-3-buten-1-yl}-propane-2-sulfinamide (**5i**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (8:1)] afforded **5i** as a colorless oil (64% two steps, 100 mg). $[\alpha]_D^{25}$ = −88.8 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.11 (s, 9H), 2.04 (s, 3H), 2.27−2.55 (m, 2H), 3.59 (br, 1H), 4.66 (br, 1H), 4.81 (s, 1H), 5.08−5.12 (m, 2H), 5.18 (s, 1H), 5.59−5.74 (m, 1H), 7.04 (d, *J* = 7.0 Hz, 1H), 7.16−7.19 (m, 2H), 7.30 (d, *J* = 7.1 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.5 ($3CH_3$), 25.7 (CH_3), 43.8 (CH_2), 52.5 (*CH*), 55.5 (*C*), 115.8 (CH_2), 118.9 (CH_2), 127.0 (*CH*), 127.1 (*CH*), 128.1 (*C*), 134.6 (*CH*), 138.2 (*C*), 143.9 (*C*), 144.7 (*C*) ppm. HRMS (EI) calcd. for $C_{17}H_{25}NOS$ [M + H^+]: 292.1730, found 292.1722.

*(R_S)-Ethyl 2-{2-[(1S)-1-[(tert-butylsulfinyl)amino]-3-buten-1-yl]-phenyl}acrylate (**5j**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (3:1)] afforded **5j** as colorless oil (62% two steps, 39 mg). $[\alpha]_D^{25}$ = −99.8 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16 (s, 9H), 1.27 (t, *J* = 8.5 Hz, 3H), 2.29−2.40 (m, 1H), 2.56−2.63 (m, 1H), 3.70 (br, 1H), 4.18−4.29 (m, 2H), 4.47−4.52 (m, 1H), 5.13−5.18 (m, 2H), 5.63−5.77 (m, 1H), 5.81 (d, *J* = 1.5 Hz, 1H), 6.61 (d, *J* = 1.5 Hz, 1H), 7.12 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.27−7.28 (m, 1H), 7.31−7.37 (m, 1H), 7.44 (dd, *J* = 8.0, 1.7 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.1 (CH_3), 22.6 ($3CH_3$), 42.8 (CH_2), 52.9 (*CH*), 55.6 (*C*), 61.3 (CH_2), 119.1 (CH_2), 126.9 (*CH*), 127.1 (*CH*), 128.2 (*CH*), 129.8 (*CH*), 129.9 (CH_2), 134.5 (*CH*), 137.0 (*C*), 139.9 (*C*), 140.4 (*C*), 166.4 (*C*) ppm. HRMS (EI) calcd. for $C_{19}H_{28}NO_3S$ [M + H^+]: 350.1784, found 350.1793.

*(R_S)-N-{(S)-1-[2-(3,3-Difluoro-3-(phenylsulfonyl)-1-propen-2-yl)-phenyl]-3-buten-1-yl}-2-methylpropane-2-sulfinamide (**5k**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (2:1)] afforded **5k** as colorless oil (95%, 100 mg). $[\alpha]_D^{25}$ = −66.1 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16 (s, 9H), 2.30−2.41 (m, 1H), 2.61−2.65 (m, 1H), 3.79 (br, 1H), 4.64−4.68 (m, 1H), 5.14−5.21 (m, 2H), 5.69−5.83 (m, 1H), 6.06 (br, 1H), 6.42 (t, *J* = 1.5 Hz, 1H), 7.18−7.47 (m, 4H), 7.57−7.62 (m, 2H), 7.72−7.77 (m, 1H), 7.99 (d, *J* = 7.5 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.6 ($3CH_3$), 42.9 (CH_2), 52.8 (*CH*), 55.6 (*C*), 119.2 (CH_2), 120.5 (t, J^1_{CF} = 287.7 Hz; CF_2), 125.3 (*C*), 127.1 (*CH*), 127.5 (*CH*), 128.2 (*CH*), 129.0 (*CH*), 129.2 (2*CH*), 130.5 (t, J^3_{CF} = 6.2 Hz; CH_2), 130.6 (*CH*), 130.9 (2*CH*), 132.9 (*C*), 134.8 (*CH*), 135.2 (*CH*), 140.8 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −99.9 (d, *J* = 219.1 Hz, 1F; C*F*F), −94.8 (d, *J* = 205.6 Hz, 1F; CF*F*) ppm. HRMS (EI) calcd. for $C_{23}H_{28}F_2NO_3S_2$ [M + H^+]: 468.1469, found 468.1468.

General Procedure for the Protecting Group Exchange. Hydrogen chloride (2.9 mmol, 4.0 equiv, 4 M solution in 1,4-dioxane) was added at room temperature to a solution of the corresponding sulfinyl amine (0.73 mmol, 1.0 equiv) in MeOH (1 M). After 30 min the deprotection was complete and the solution was concentrated to dryness. The residue was redissolved in CH_2Cl_2 (5 mL) and 2 M NaOH was added and extracted three times with dichloromethane. The combined organic layers were dried over anhydrous Na_2SO_4. Solvents were removed under reduced pressure and the crude reaction mixture was used in the next protection step without further purification.

a. N-Boc-protection. The resulting crude product was dissolved in anhydrous 1,4-dioxane (0.2 M) and treated with K_2CO_3 (1.8 mmol, 2.5 equiv) and di-*tert*-butyl dicarbonate (Boc_2O) (0.9 mmol, 1.1 equiv). The mixture was stirred at 50 °C overnight, until TLC revealed the disappearance of the free amine. The suspension was then filtered through a short pad of Celite and washed with small portions of ethyl acetate. Solvents were removed under reduced pressure and the residue was purified by means of flash chromatography on silica gel affording the desired product.

*tert-Butyl (S)-{1-[2-(3,3,3-trifluoro-1-propen-2-yl)phenyl]-3-buten-1-yl}carbamate (**6a**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (30:1)] afforded **6a** as a white solid (83%, 100 mg). $[\alpha]_D^{25}$ = −18.5 (*c* 1.0; $CHCl_3$). mp 30−32 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.39 (s, 9H), 2.41−2.47 (m, 2H), 4.78 (br, 1H), 4.92 (br, 1H), 5.04- 5.12 (m, 2H), 5.60−5.74 (m, 2H), 6.20 (d, *J* = 3.0 Hz, 1H), 7.25−7.38 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.3 ($3CH_3$), 41.0 (CH_2), 50.4 (*CH*), 50.5 (*CH*), 79.4 (*C*), 118.8 (CH_2), 122.9 (q, J^1_{CF} = 271.8, CF_3), 124.4 (q, J^3_{CF} = 2.2, CH_2), 125.9 (*CH*), 126.8 (*CH*), 129.2 (*CH*), 130.1 (*CH*), 132.5 (*C*), 134.0 (*CH*), 141.5 (*C*), 154.7 (*C*), ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.0 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{18}H_{22}F_3NO_2$ [M + H^+]: 342.1675, found 342.1673. HPLC (Chiralcel OD-H, 98:2

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hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 5.00 min, t_R(minor) = 4.56 min.

*tert-Butyl (S)-{1-[5-chloro-2-(3,3,3-trifluoro-1-propen-2-yl)-phenyl]-3-buten-1-yl}carbamate (**6b**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (30:1)] afforded **6b** as a colorless oil (55%, 90 mg). $[\alpha]_D^{25}$ = −38.2 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.40 (s, 9H), 2.30−2.48 (m, 2H), 4.83−4.89 (m, 2H), 5.09−5.14 (m, 2H), 5.60−5.71 (m, 1H), 5.74 (br, 1H), 6.23 (d, *J* = 1.5 Hz, 1H), 7.18 (d, *J* = 9.0 Hz, 1H), 7.23 (dd, *J* = 9.0, 3.0 Hz, 1H), 7.35 (d, *J* = 3.0 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.3 ($3CH_3$), 40.9 (CH_2), 50.5 (d, J^4_{CF} = 1.4; *C*H), 79.7 (*C*), 118.6 (CH_2), 122.7 (q, J^1_{CF} = 273.8; CF_3), 125.2 (q, CH_2, J^3_{CF} = 4.7), 126.3 (*C*H), 127.0 (*C*H), 130.7 (*C*), 131.3 (*C*H), 133.5 (*C*H), 135.2 (*C*), 135.7 (*C*), 143.9 (*C*), 154.7 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −66.9 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{14}H_{13}ClF_3NO_2$ [M + H^+]: 320.0660, found 320.0658. HPLC (Chiralcel OD-H, 98:2 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 4.01 min, t_R(minor) = 4.24 min.

*tert-Butyl (S)-{1-[4-fluoro-2-(3,3,3-trifluoro-1-propen-2-yl)-phenyl]-3-buten-1-yl}carbamate (**6c**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (20:1)] afforded **6c** as a yellow solid (68%, 105 mg). $[\alpha]_D^{25}$ = −12.2 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.38 (s, 9H), 2.37−2.46 (m, 2H), 4.81−4.89 (m, 2H), 5.04−5.11 (m, 2H), 5.58−5.22 (m, 1H), 5.78 (br, 1H), 6.23 (d, *J* = 1.5 Hz, 1H), 6.95 (dd, *J* = 9.3, 2.7 Hz, 1H), 7.07 (dd, *J* = 8.1, 2.7 Hz, 1H), 7.33 (dd, *J* = 8.7, 3.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.3 ($3CH_3$), 41.0 (CH_2), 50.1 (*C*H), 75.5 (*C*), 116.2 (d, J^2_{CF} = 21.0; *C*H), 116.7 (d, J^2_{CF} = 22.1; *C*H), 118.3 (CH_2), 122.7 (q, J^1_{CF} = 273.9; CF_3), 125.0 (d, J^3_{CF} = 2.0; *C*H), 127.7 (d, J^2_{CF} = 83.3; *C*H), 133.7 (*C*H), 134.2 (*C*), 135.5 (d, J^3_{CF} = 31.5; *C*), 137.6 (d, J^4_{CF} = 3.1; *C*), 154.7 (*C*), 160.9 (d, J^1_{CF} = 271.8; *C*H) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −115.7 (ddd, *J* = 14.4, 8.5, 5.6 Hz, 1F; *C*F), −66.9 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{18}H_{21}F_4NO_2$ [M + H^+]: 360.1581, found 360.1573. HPLC (Chiralcel OD-H, 99.5:0.5 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 8.96 min, t_R(minor) = 9.82 min.

*tert-Butyl (S)-{1-[6-(3,3,3-trifluoro-1-propen-2-yl)benzo[d][1,3]-dioxol-5-yl]-3-buten-1-yl}carbamate (**6d**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (10:1)] afforded **6d** as colorless oil (67%, 120 mg). $[\alpha]_D^{25}$ = −19.2 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25 (s, 9H), 2.25 (t, *J* = 6.9 Hz, 2H), 4.63−4.70 (m, 2H), 4.89−4.97 (m, 2H), 5.45−5.57 (m, 2H), 5.83 (s, 2H), 6.04 (d, *J* = 1.5 Hz, 1H), 6.55 (s, 1H), 6.68 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.3 ($3CH_3$), 41.1 (CH_2), 50.7 (*C*H), 79.4 (*C*), 101.4 (CH_2), 105.9 (*C*H), 109.7 (*C*H), 118.0 (CH_2), 122.9 (q, J^1_{CF} = 279.3 Hz, CF_3), 124.7 (q, J^3_{CF} = 2.3 Hz; CH_2), 124.7 (*C*), 125.6 (*C*), 133.9 (*C*H), 135.8 (*C*), 136.3 (*C*), 146.7 (*C*), 148.4 (*C*), 154.7 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −66.1 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{19}H_{22}F_3NO_4$ [M + H^+]: 386.1574, found 386.1580. HPLC (Chiralpak IC, 98:2 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 7.46 min, t_R(minor) = 6.65 min.

*tert-Butyl (S)-{1-[5-methoxy-2-(3,3,3-trifluoro-1-propen-2-yl)-phenyl]-3-buten-1-yl}carbamate (**6e**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (10:1)] afforded **6e** as a colorless oil (84%, 105 mg). $[\alpha]_D^{25}$ = −26.3 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.39 (s, 9H), 2.34- 2.50 (m, 2H), 3.81 (s, 3H), 4.81−4.90 (m, 2H), 5.04−5.12 (m, 2H), 5.60−5.74 (m, 2H), 6.17 (d, *J* = 1.5 Hz, 1H), 6.79 (dd, *J* = 8.4, 2.7 Hz, 1H), 6.88 (d, *J* = 2.7 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 1H), ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.3 ($3CH_3$), 40.9 (CH_2), 50.7 (CH), 55.2 (OCH_3), 79.4 (*C*), 111.8 (2CH), 118.0 (CH_2), 122.9 (q, CF_3, J^1_{CF} = 268.8 Hz), 124.5 (q, CH_2, J^3_{CF} = 3.5 Hz), 124.7 (*C*), 131.2 (CH), 134.0 (CH), 136.2 (d, *C*, J^3_{CF} = 28.8 Hz), 143.1 (*C*), 154.7 (*C*), 160.1 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −66.1 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{19}H_{24}F_3NO_3$ [M + H^+]: 372.1781, found 372.1783. HPLC (Chiralpak IC, 98:2 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 6.67 min, t_R(minor) = 5.74 min.

*tert-Butyl (S)-{1-[3-(3,3,3-trifluoro-1-propen-2-yl)thiophen-2-yl]-3-but-3-en-1-yl}carbamate (**6f**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (20:1)] afforded **6f** as a colorless oil (64%, 160 mg). $[\alpha]_D^{25}$ = −4.5 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.41 (s, 3H), 2.47−2.58 (m, 2H), 4.82 (s, 1H), 5.07−5.13 (m, 3H), 5.63−5.72 (m, 1H), 5.76 (s, 1H), 6.12 (d, *J* = 1.2 Hz, 1H), 6.96 (dd, *J* = 5.1, 0.9 Hz, 1H), 7.20 (d, *J* = 5.4 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.3 ($3CH_3$), 42.0 (CH_2), 48.6 (*C*H), 79.8 (*C*), 118.6 (CH_2), 122.1 (q, J^1_{CF} = 267.0 Hz; CF_3), 123.1 (*C*H), 123.8 (CH_2), 128.2 (*C*H), 130.7 (*C*), 133.2 (*C*H), 146.1 (*C*), 154.6 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −66.7 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{16}H_{20}F_3NO_2S$ [M + H^+]: 348.1240, found 348.1249. HPLC (Chiralpcel OD-H, 98:2 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 4.68 min, t_R(minor) = 4.37 min.

*tert-Butyl {(1S,2S)-2-methyl-1-[6-(3,3,3-trifluoro-1-propen-2-yl)-benzo[d][1,3]dioxol-5-yl]-3-buten-1-yl}carbamate (**6g**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (10:1)] afforded **6g** as colorless oil (74%, 95 mg). $[\alpha]_D^{25}$ = −39.8 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (d, *J* = 6.9 Hz, 3H), 1.38 (s, 9H), 2.44 (dd, *J* = 21.0, 13.8 Hz, 1H), 4.7 (s, 2H), 5.11−5.04 (m, 2H), 5.83−5.71 (m, 2H), 5.96 (dd, *J* = 3.3, 1.2 Hz, 2H), 6.19 (s, 1H), 6.72 (s, 1H), 6.76 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 17.2 (CH_3), 21.5 (*C*H), 28.3 ($3CH_3$), 43.9 (*C*H), 54.7 (*C*H), 79.2 (*C*), 101.4 (CH_2), 106.2 (*C*H), 109.5 (*C*H), 116.4 (CH_2), 122.9 (q, J^1_{CF} = 274.3 Hz; CF_3), 124.7 (*C*), 125.4 (CH_2), 128.4 (*C*), 135.3 (*C*), 146.2 (*C*), 148.3 (*C*), 154.7 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −66.4 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{20}H_{24}F_3NO_4$ [M + Na]: 422.1550, found 422.1561. HPLC (Chiralpak IC, 98:2 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 6.50 min, t_R(minor) = 5.97 min.

*tert-Butyl (S)-{1-[2-(3,3,4,4,4-pentafluoro-1-buten-2-yl)phenyl]-3-buten-1-yl}carbamate (**6h**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (10:1)] afforded **6h** as colorless oil (88%, 80 mg). $[\alpha]_D^{25}$ = −19.0 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.32 (s, 9H), 2.38−2.40 (m, 2H), 4.69 (br, 1H), 4.79 (br, 1H), 4.96−5.02 (m, 2H), 5.56−5.64 (m, 1H), 5.75 (s, 1H), 6.14 (s, 1H), 7.11−7.13 (m, 1H), 7.16−7.20 (m, 1H), 7.28−7.33 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.3 ($3CH_3$), 41.1 (CH_2), 50.8 (*C*H), 79.3 (*C*), 112.5 (tq, J^1_{CF} = 251.1 Hz, J^2_{CF} = 39.4 Hz; CF_2CF_3), 117.9 (CH_2), 119.4 (qt, J^1CF= 287.7 Hz, J^2CF= 36.6 Hz; CF_2CF_3), 125.9 (*C*H), 126.8 (*C*H), 127.7 (CH_2), 129.2 (*C*H), 130.3 (*C*H), 133.1 (*C*), 134.1 (*C*H), 135.9 (*C*), 154.6 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −112.7 (br, 2F; CF_2), −82.9 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{19}H_{22}F_5NO_2$ [M + H^+]: 392.1643, found 392.1637. HPLC (Chiralcel OD-H, 98:2 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 4.68 min, t_R(minor) = 4.28 min.

b. N-Acetyl-protection. The crude residue from the chiral auxiliary deprotection described above was redissolved in anhydrous CH_2Cl_2 (8 mL), and Ac_2O (1.2 mmol, 1.5 equiv), Et_3N (1.62 mmol, 2 equiv) and DMAP (0.162 mmol, 0.8 equiv) were successively added at room temperature. The mixture was stirred at room temperature for 16 h. At this time, the reaction was hydrolyzed with aq. NH_4Cl and extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by means of flash chromatography on silica gel.

*(S)-N-{1-[2-(3,3,3-Trifluoro-1-propen-2-yl)phenyl]-3-buten-1-yl}-acetamide (**6a′**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (2:1)] afforded **6a′** as colorless oil (74%, 90 mg). $[\alpha]_D^{25}$ = −41.7 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.90 (s, 3H), 2.43−2.48 (m, 2H), 5.02−5.09 (m, 2H), 5.15−5.22 (m, 1H), 5.60−5.73 (m, 1H), 5.76 (dd, *J* = 1.3, 1.3 Hz, 1H), 5.98 (d, *J* = 7.3 Hz, 1H), 6.19 (dd, *J* = 1.5, 1.5 Hz, 1H), 7.23−7.28 (m, 2H), 7.32−7.37 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 23.1 (CH_3), 40.5 (CH_2), 49.5 (CH), 118.0 (CH_2), 123.2 (q, J^1_{CF} = 275.5 Hz; CF_3), 124.6 (q, J^3_{CF} = 6.0 Hz; CH_2), 126.0 (CH), 126.9 (CH), 129.1 (CH), 130.1 (CH), 132.7 (*C*), 134.1 (CH), 136.1 (q, J^2_{CF} = 34.0 Hz; *C*), 141.1 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.0 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{15}H_{16}F_3NO$ [M + H^+]: 284.1257, found 284.1253. HPLC (Chiralcel OD-H, 95:5 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 9.52 min, t_R(minor) = 8.12 min.

*(S)-N-{1-[3-(3,3,3-Trifluoro-1-propen-2-yl)thiophen-2-yl]-3-buten-1-yl}acetamide (**6f′**).* Flash chromatography of the crude reaction

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product [*n*-hexane-EtOAc (2:1)] afforded **6f′** as colorless oil (80%, 190 mg). $[\alpha]_D^{25}$ = −28.7 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.18 (d, *J* = 5.2 Hz, 1H), 6.93 (dd, *J* = 5.2, 1.1 Hz, 1H), 6.26 (d, *J* = 6.9 Hz, 1H), 6.09 (dd, *J* = 1.5, 1.3 Hz, 1H), 5.77 (dd, *J* = 1.5, 1.3 Hz, 1H), 5.59−5.73 (m, 1H), 5.4 (q, *J* = 7.5 Hz, 1H), 5.11−5.03 (m, 2H), 2.62−2.44 (m, 2H), 1.02 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.9 (CH_3), 41.6 (CH_2), 47.7 (*C*H), 118.5 (CH_2), 122.8 (q, J^1_{CF} = 275.5 Hz; CF_3), 123.2 (*C*H), 123.9 (q, J^3_{CF} = 5.5 Hz, CH_2), 128.1 (*C*H), 131.0 (*C*), 132.8 (q, J^2_{CF} = 32.9 Hz, *C*), 133.2 (*C*H), 145.1 (*C*), 169.1 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −67.2 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{13}H_{14}F_3NOS$ [M + H^+]: 290.0821, found 290.0831. HPLC (Chiralcel OD-H, 95:5 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 9.00 min, t_R(minor) = 8.14 min.

*(S)-N-(1-{2-[3,3-Difluoro-3-(phenylsulfonyl)-1-propen-2-yl]-phenyl}-3-buten-1-yl)acetamide (**6k**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (1:1)] afforded **6k** as colorless oil (72%, 90 mg). $[\alpha]_D^{25}$ = −14.5 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.90 (s, 3H), 2.49−2.54 (m, 2H), 5.02−5.19 (m, 3H), 5.61−5.74 (m, 2H), 6.06 (br, 1H), 6.41 (br, 1H), 7.27−7.42 (m, 3H), 7.47−7.49 (m, 1H), 7.57−7.62 (m, 2H), 7.71−7.77 (m, 1H), 7.99 (d, *J* = 7.8 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 23.2 (CH_3), 31.5 (CH_2), 40.6 (CH_2), 50.0 (*C*H), 117.9 (CH_2), 120.5 (t, J^1_{CF} = 172.8 Hz; CF_2), 125.8 (*C*H), 127.0 (*C*H), 129.1 (*C*H), 129.2 (*C*H), 130.7 (*C*), 130.9 (*C*H), 132.9 (*C*), 133.6 (*C*), 134.2 (*C*H), 135.2 (*C*H), 141.2 (*C*), 169.0 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −99.7 (s, 1F; C*F*F), −93.1 (s, 1F; CF*F*) ppm. HRMS (EI) calcd. for $C_{21}H_{22}F_2NO_3S$ [M + H^+]: 406.1288, found 406.1284.

General Procedure for the RCM Reaction. To a solution of the corresponding homoallylamine **5i,j** or **6a−h,k,a′,f′** (0.4 mmol, 1.0 equiv) in toluene (for R′ = R_F) or CH_2Cl_2 (for R′ = CH_3, CO_2Et) (8 mL, 0.05M), second generation Grubbs catalyst [Ru−II] (0.02 mmol, 5 mol %) (for **6a−f,k**) or second generation Hoveyda−Grubbs catalyst [Ru−III] (0.02 mmol, 5 mol %) (for **5i,j** and **6a′,f′**) was added. The reaction mixture was stirred approximately 4 h at 100 °C (for compounds **6**) or room temperature (for compounds **5**). After that time, the reaction mixture was concentrated under vacuum and purified by means of flash chromatography on silica gel.

*tert-Butyl (S)-[4-(trifluoromethyl)-1,2-dihydronaphthalen-1-yl]-carbamate (**7a**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (20:1)] afforded **7a** as a white solid (67%, 80 mg). $[\alpha]_D^{25}$ = −16.3 (*c* 1.0; $CHCl_3$). mp 39−41 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.45 (s, 9H), 2.66 (br, 2H), 4.79−4.94 (m, 2H), 6.64−6.67 (m, 1H), 7.32−7.35 (m, 2H), 7.37−7.40 (m, 1H), 7.45−7.47 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.5 ($3CH_3$), 29.6 (CH_2), 47.2 (*C*H), 79.8 (*C*), 123.3 (q, J^1_{CF} = 273.1 Hz; CF_3), 124.6 (*C*H), 127.4 (2*C*), 127.6 (*C*H), 128.3 (*C*H), 129.6 (q, J^3_{CF} = 5.8 Hz; *C*H), 125.6 (*C*), 135.3 (*C*), 154.9 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −64.3 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{16}H_{18}F_3NO_2$ [M + H^+]: 314.1362, found 314.1347. HPLC (Chiralcel OD-H, 99.5:0.5 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 17.92 min, t_R(minor) = 16.40 min.

*tert-Butyl (S)-[7-chloro-4-(trifluoromethyl)-1,2-dihydronaphthalen-1-yl]carbamate (**7b**).* Flash chromatography of the crude reaction product [*n*-hexane- Et_2O (20:1)] afforded **7b** as a white solid (74%, 75 mg). $[\alpha]_D^{25}$ = −3.43 (*c* 1.0; $CHCl_3$). mp 85−87 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.46 (s, 9H), 2.60−2.65 (m, 2H), 4.80−4.92 (m, 2H), 6.64−6.68 (m, 2H), 7.27−7.31 (m, 1H), 7.36 (d, *J* = 1.8 Hz, 1H), 7.39 (d, *J* = 2.0 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.3 ($3CH_3$), 29.5 (CH_2), 47.1 (*C*H), 80.1 (*C*), 123.1 (q, J^1_{CF} = 277.8 Hz, CF_3), 125.9 (*C*H), 127.4 (*C*H), 127.7 (*C*), 128.3 (*C*H), 129.9 (q, J^3_{CF} = 5.0 Hz, *C*H), 134.7 (*C*), 137.4 (*C*), 154.9 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −64.5 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{16}H_{17}ClF_3NO_2$ [M + H^+]: 348.0973, found 348.0975. HPLC (Chiralcel OD-H, 99:1 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 13.45 min, t_R(minor) = 11.37 min.

*tert-Butyl (S)-[6-fluoro-4-(trifluoromethyl)-1,2-dihydronaphthalen-1-yl]carbamate (**7c**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (20:1)] afforded **7c** as a colorless oil (66%, 60 mg). $[\alpha]_D^{25}$ = −16.2 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.44 (s, 9H), 2.57−2.74 (m, 2H), 4.76−4.91 (m, 2H), 6.72 (t, *J* = 3.3 Hz, 2H), 7.01 (ddd, *J* = 10.8, 8.4, 2.7 Hz, 1H), 7.15−7.19 (m, 1H), 7.40 (dd, *J* = 8.4, 5.7 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.3 ($3CH_3$), 29.8 (CH_2), 46.5 (*C*H), 79.9 (*C*), 111.8 (d, J^3_{CF} = 2.2 Hz; *C*H), 112.2 (*C*H), 115.4 (*C*H), 115.7 (*C*H), 123.0 (q, J^1_{CF} = 277.8 Hz; CF_3), 127.9 (q, J^2_{CF} = 24.5 Hz, *C*), 129.2 (q, J^3_{CF} = 7.6 Hz, *C*), 131.0 (*C*), 154.8 (*C*), 162.4 (d, J^1_{CF} = 241.6 Hz; *C*F) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −64.6 (s, 3F; CF_3), −113.2 (dd, J^1= −15.2 Hz, J^2= −9.0 Hz, 1F; C*F*) ppm. HRMS (EI) calcd. for $C_{16}H_{17}F_4NO_2$ [M + H^+]: 332.1312, found 332.1310. HPLC (Chiralcel OD-H, 99:1 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 12.44 min, t_R(minor) = 11.69 min.

*tert-Butyl (S)-[8-(trifluoromethyl)-5,6-dihydronaphtho[2,3-d]-[1,3]dioxol-5-yl]carbamate (**7d**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (5:1)] afforded **7d** as colorless oil (80%, 58 mg). $[\alpha]_D^{25}$ = −2.05 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.44 (s, 9H), 2.54−2.68 (m, 2H), 4.62−4.64 (m, 1H), 4.77 (s, 1H), 5.97 (s, 2H), 6.53−6.56 (m, 1H), 6.89 (s, 1H), 6.96 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.4 ($3CH_3$), 29.6 (CH_2), 47.3 (*C*H), 79.8 (*C*H), 101.4 (CH_2), 105.4 (*C*H), 108.5 (*C*), 123.3 (q, J^1_{CF} = 277.8 Hz; CF_3), 127.5 (q, J^3_{CF} = 5.7 Hz; *C*H), 128.0 (*C*), 128.4 (*C*), 130.1 (*C*), 147.5 (*C*), 147.6 (*C*), 154.8 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −63.9 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{17}H_{19}F_3NO_4$ [M + H^+]: 358.1261, found 358.1259. HPLC (Chiralpak IC, 98:2 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 12.93 min, t_R(minor) = 9.66 min.

*tert-Butyl (S)-[7-methoxy-4-(trifluoromethyl)-1,2-dihydronaphthalen-1-yl]carbamate (**7e**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (7:1)] afforded **7e** as a white solid (77%, 53 mg). $[\alpha]_D^{25}$ = −5.44 (*c* 1.0; $CHCl_3$). mp 80−82 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.45 (s, 9H), 2.61 (br, 2H), 3.83 (s, 3H), 4.78−4.86 (m, 2H), 6.49−6.52 (m, 1H), 6.84 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.94 (d, *J* = 2.7 Hz, 1H), 7.40 (dd, *J* = 8.7, 1.8 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.4 ($3CH_3$), 29.6 (CH_2), 47.6 (*C*H), 55.4 (OCH_3), 79.8 (*C*), 79.8 (*C*), 113.3 (2*C*H), 120.3 (*C*), 123.4 (q, J^1_{CF} = 273.0 Hz; CF_3), 126.1 (*C*H), 126.7 (*C*), 128.2 (d, J^2_{CF} = 29.8 Hz; *C*), 137.4 (*C*), 154.9 (*C*), 159.9 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −63.9 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{17}H_{20}F_3NO_3$ [M + H^+]: 344.1468, found 344.1460. HPLC (Chiralpak IC, 98:2 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 10.54 min, t_R(minor) = 7.88 min.

*tert-Butyl (S)-[4-(trifluoromethyl)-6,7-dihydrobenzo[b]thiophen-7-yl]carbamate (**7f**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (12:1)] afforded **7f** as a yellow solid (68%, 99 mg). $[\alpha]_D^{25}$ = −35.4 (*c* 1.0; $CHCl_3$). mp 81−83 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.44 (s, 9H), 2.74−2.84 (m, 2H), 4.90 (br, 1H), 5.17−5.94 (m, 1H), 6.38−6.42 (m, 1H), 7.06 (dd, *J* = 5.4, 1.8 Hz, 1H), 7.24 (d, *J* = 5.1 Hz, 1H), ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.7 ($3CH_3$), 31.5 (CH_2), 44.1 (*C*H), 80.0 (*C*), 117.6 (*C*), 121.2 (*C*), 124.3 (*C*H), 125.3 (*C*H), 125.5 (*C*H), 129.3 (*C*), 137.5 (*C*), 154.5 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −66.6 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{14}H_{16}F_3NO_2S$ [M + H^+]: 320.0927, found 320.0922. HPLC (Chiralpak IC, 98:2 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 8.08 min, t_R(minor) = 7.04 min.

*tert-Butyl [(5S,6S)-6-methyl-8-(trifluoromethyl)-5,6-dihydronaphtho[2,3-d][1,3]dioxol-5-yl]carbamate (**7g**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (20:1)] afforded **7g** as a white solid (42%, 30 mg). $[\alpha]_D^{25}$ = −32.5 (*c* 1.0; $CHCl_3$). mp 135−137 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.2 (d, *J* = 7.2 Hz, 3H), 1.44 (s, 9H), 2.74 (s, 1H), 4.62−4.64 (m, 1H), 4.77 (s, 1H), 5.97 (s, 2H), 6.28−6.29 (m, 1H), 6.89 (s, 1H), 6.96 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.2 (CH_3), 28.3 ($3CH_3$), 32.2 (*C*H), 51.5 (*C*H), 79.7 (*C*), 101.4 (CH_2), 105.3 (*C*H), 108.6 (*C*H), 120.6 (*C*), 123.3 (q, J^1_{CF} = 277.8 Hz; CF_3), 127.7 (q, J^2_{CF} = 29.6 Hz; *C*), 131.2 (*C*), 133.8 (q, J^3_{CF} = 8.2 Hz; *C*H), 147.5 (*C*), 147.7 (*C*), 155.3 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −64.3 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{18}H_{20}F_3NO_4$ [M + H^+]: 372.1417, found 372.1402. HPLC (Chiralpak IC, 98:2 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 9.49 min, t_R(minor) = 7.44 min.

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*(S)-N-[4-(Trifluoromethyl)-1,2-dihydronaphthalen-1-yl]-acetamide (**7a′**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (2:1)] afforded **7a′** as colorless oil (42%, 54 mg). $[\alpha]_D^{25}$ = −2.0 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.96 (s, 3H), 2.58−2.79 (m, 2H), 5.19−5.25 (m, 1H), 5.71 (br, 1H), 6.64−6.68 (m, 1H), 7.32−7.39 (m, 3H), 7.48−7.51 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 23.4 (CH_3), 29.2 (CH_2), 45.8 (*C*H), 123.5 (q, J^1_{CF} = 271.1 Hz; CF_3), 124.7 (q, J^4_{CF} = 2.2 Hz; *C*H), 127.4 (*C*), 128.1 (*C*H), 128.6 (*C*H), 129.1 (*C*H), 129.7 (q, J^3_{CF} = 6.2 Hz; *C*H), 134.6 (*C*), 169.2 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −64.3 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{13}H_{12}F_3NO$ [M + H$^+$]: 256.0944, found 256.0956. HPLC (Chiralcel OD-H, 95:5 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 19.70 min, t_R(minor) = 15.40 min.

*(S)-N-[4-(Trifluoromethyl)-6,7-dihydrobenzo[b]thiophen-7-yl]-acetamide (**7f′**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (4:1)] afforded **7f′** as a white solid (44%, 65 mg). $[\alpha]_D^{25}$ = −6.5 (*c* 1.0; $CHCl_3$). mp 133−135 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.94 (s, 3H), 2.74−2.78 (m, 2H), 5.33−5.40 (m, 1H), 5.96 (d, *J* = 9.3 Hz, 1H), 6.39−6.42 (m, 1H), 7.08 (dd, *J* = 5.1, 1.8 Hz, 1H), 7.26 (d, *J* = 5.1 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 23.1 (CH_3), 30.7 (CH_2), 42.1 (*C*H), 122.5 (q, J^1_{CF} = 268.4 Hz; CF_3), 123.9 (*C*H), 124.7 (*C*), 125.1 (q, J^3_{CF} = 4.4 Hz; *C*H), 125.2 (*C*H), 126.1 (q, J^2_{CF} = 32.4 Hz; *C*), 129.6 (*C*), 136.6 (*C*), 169.1 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −66.5 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $C_{11}H_{10}F_3NOS$ [M + H$^+$]: 262.0508, found 262.0505. HPLC (Chiralcel OD-H, 95:5 hexane/iPrOH, 1 mL min^{-1}, 240 nm) t_R(major) = 20.20 min, t_R(minor) = 18.17 min.

*tert-Butyl (S)-[4-(perfluoroethyl)-1,2-dihydronaphthalen-1-yl]-carbamate (**7h**).* Flash chromatography of the crude reaction product [*n*-hexane-Et_2O (15:1)] afforded **7h** as colorless oil (80%, 20 mg). $[\alpha]_D^{25}$ = −15.8 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.46 (s, 9H), 2.64−2.66 (m, 2H), 4.74−4.77 (m, 1H), 4.85−4.92 (m, 1H), 6.68 (t, *J* = 6.03 Hz, 1H), 7.30−7.33 (m, 2H), 7.38−7.41 (m, 1H), 7.50−7.53 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.4 ($3CH_3$), 29.9 (CH_2), 47.4 (*C*H), 79.9 (*C*), 113.5−121.6 (C_2F_5), 125.4 (*C*H), 127.4 (*C*H), 127.9 (*C*), 128.2 (*C*H), 128.9 (*C*H), 133.3 (t, J^3_{CF} = 10.0 Hz; *C*H), 135.7 (*C*), 154.9 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −111.2 (q, *J* = 285 Hz, 2F; CF_2), −83.3 (s, 3F; CF_3) ppm. HRMS (EI) calcd. for $NaC_{17}H_{18}F_5NO_2$ [M + Na$^+$]: 386.1150, found 386.1138. HPLC (Chiralpak IC, 98:2 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 8.20 min, t_R(minor) = 7.37 min.

*(R_S)-2-Methyl-N-[(S)-4-methyl-1,2-dihydronaphthalen-1-yl]-propane-2-sulfinamide (**7i**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (2:1)] afforded **7i** as a colorless oil (72%, 25 mg). $[\alpha]_D^{25}$ = −6.8 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.14 (s, 9H), 2.04 (s, 3H), 2.50−2.71 (m, 2H), 3.36 (d, *J* = 9.0 Hz, 1H), 4.37−4.44 (m, 1H), 5.78 (br, 1H), 7.20−7.34 (m, 4H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 19.1 (CH_3), 22.6 ($3CH_3$), 32.6 (CH_2), 55.0 (*C*H), 56.1 (*C*), 122.1 (*C*H), 123.4 (*C*H), 126.7 (*C*H), 127.2 (*C*H), 127.9 (*C*H), 132.2 (*C*), 134.9 (*C*), 135.9 (*C*) ppm. HRMS (EI) calcd. for $C_{15}H_{21}NOS$ [M + H$^+$]: 264.1417, found 264.1412.

*(R_S)-Ethyl-(4S)-4-[(tert-butylsulfinyl)amino]-3,4-dihydronaphthalene-1-carboxylate (**7j**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (1:1)] afforded **7j** as a colorless oil (87%, 15 mg). $[\alpha]_D^{25}$ = −4.2 (*c* 1.0; $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (s, 9H), 1.40 (t, *J* = 7.0 Hz, 3H), 2.78−2.83 (m, 2H), 3.34 (d, *J* = 9.2 Hz, 1H), 4.32 (q, *J* = 7.0 Hz, 2H), 4.44−4.51 (m, 1H), 7.07−7.10 (m, 1H), 7.29−7.40 (m, 3H), 7.89 (d, *J* = 7.5 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.2 (CH_3), 22.6 ($3CH_3$), 32.6 (CH_2), 54.1 (*C*H), 56.3 (*C*), 60.8 (CH_2), 126.7 (*C*H), 126.9 (*C*H), 128.1 (*C*H), 128.2 (*C*H), 130.0 (*C*), 130.7 (*C*), 135.6 (*C*H), 135.8 (*C*), 165.9 (*C*) ppm. HRMS (EI) calcd. for $C_{17}H_{23}NO_3S$ [M + H$^+$]: 322.1471, found 322.1473.

*(S)-N-{4-[Difluoro(phenylsulfonyl)methyl]-1,2-dihydronaphthalen-1-yl}acetamide (**7k**).* Flash chromatography of the crude reaction product [*n*-hexane-EtOAc (3:1)] afforded **7k** as a white solid (40%, 15 mg). $[\alpha]_D^{25}$ = −7.45 (*c* 1.0; $CHCl_3$). mp 70−72 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.94 (s, 3H), 2.57−2.63 (m, 1H), 2.79−2.86 (m, 1H), 5.19 (m, 1H), 6.13 (d, *J* = 8.1 Hz, 1H), 6.75−6.77 (m, 1H), 7.32−7.35 (m, 3H), 7.63−7.81 (m, 4H), 7.99−8.02 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 23.3 (CH_3), 29.9 (CH_2), 46.2 (*C*H), 122.3 (t, J^1_{CF} = 288.4 Hz; CF_2), 126.1 (t, J^2_{CF} = 19.4 Hz; *C*) 126.3−126.4 (*C* + *C*H), 127.8 (*C*H), 128.4 (*C*H), 129.1 (*C*H), 129.3 (2*C*H), 130.7 (2*C*H), 132.9 (*C*), 135.1 (*C*H), 135.3 (*C*H), 136.5 (t, J^3_{CF} = 10.0 Hz; *C*), 169.4 (*C*) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz) δ −96.3 (dd, *J* = 229.0, 5.1 Hz; *CF*F), 99.2 (d, *J* = 228.7 Hz; *CF*F) ppm. HRMS (EI) calcd. for $C_{19}H_{18}F_2NO_3S$ [M + H$^+$]: 378.0970, found 378.0955. HPLC (Chiralcel ODH, 80:20 hexane/iPrOH, 1 mL min-1, 240 nm) t_R(major) = 9.73 min, t_R(minor) = 8.45 min.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01590.

^{1}H, ^{13}C and ^{19}F NMR spectra for all new compounds, ^{1}H for known products, and HPLC chromatograms (PDF)

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Notes

The authors declare no competing financial interest.

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