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# Stereocontrolled Fluorobenzylation of Vinyl Sulfones and α,β-Unsaturated Esters Mediated by a Remote Sulfinyl Group. Synthesis of Functionalized Enantiomerically Pure Benzylic Fluorides

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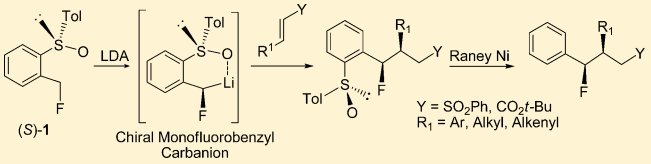
Supporting Information

**ABSTRACT:** A sulfinyl group in an *ortho* position confers enough chemical and configurational stability to monofluorobenzylcarbanions to evolve in a completely stereoselective way in their reactions with β-substituted vinyl sulfones and α,β-unsaturated esters. Reactions afford easily separable mixtures of two epimers differing in the configuration of the center derived from the Michael acceptor (up to 98% de). They can be easily converted into enantiomerically pure γ-fluorinated γ-phenylsulfones and γ-phenylesters bearing two chiral centers.



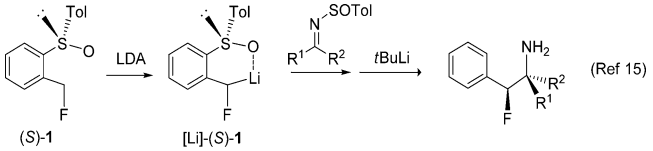

## INTRODUCTION

A fluorine atom, because of its high electronegativity and small size, is capable of conferring exceptional chemical and biological properties to the organic molecules to which it is bonded.[1] As a consequence, even though fluorinated compounds occur rarely in nature, the presence of fluorine atoms in biologically active molecules[2] confers them important roles in pharmaceutical[3] and agrochemical research.[4] Moreover, fluorine-containing compounds have been employed as liquid crystals, dyes, surfactants, plastics, elastomers, membranes, and many other materials[5] and as tracers for positron emission tomography.[6] All of these applications have required the development of synthetic methodologies able to introduce fluorinated moieties, many times in an asymmetric manner.[7]

Whereas the chemistry of trifluoro- and difluoroalkyl derivatives has been studied in some detail,[7a,8] the synthesis and reactivity of the corresponding monofluoroalkyl derivatives are only recently emerging and still remain a challenging task nowadays. Two main strategies have been developed for preparing monofluoroalkyl derivatives. The first one, involving the creation of the C−F bonds from C−H or C−Y bonds by using electrophilic fluorination reagents,[7d,9] has some disadvantages associated with the use of complex and potentially toxic reagents. The second strategy, based on the use of monofluorinated carbanions as nucleophiles, has emerged as the preferred one in past years, especially from the contributions of Prakash and Olah,[10] Hu,[11] and Shibata and Toru.[12] However, the low thermal stability of fluorinated carbanions determines that these strategies need to incorporate electron-withdrawing groups (usually a sulfonyl functionality) to the carbanionic center,[10−12] the elimination of which usually produces monofluoromethyl derivatives.[13] As this strategy precludes the preparation of compounds with the fluorine atom directly bonded to stereogenic carbons,[14] the synthesis of stereogenic monofluorinated benzyl carbons remained a subject for improvement in fluorocompound chemistry.

We have recently described that an *ortho*-sulfinyl group at (*S*)-**1**[15] is able to provide enough chemical and configurational stability to the fluorinated benzylcarbanion obtained with LDA to react with homochiral *N*-sulfinylimines in an almost complete stereoselective manner, thus providing the first monofluorobenzylation reagent for the creation of chiral monofluorinated carbons. These reactions are a typical example of double asymmetric synthesis,[16] and the use of reagents with the same configuration at the sulfur atom (matched pair) allowed the synthesis of enantiopure *anti*-β-fluorinated β-phenylethylamines (Scheme 1).

**Scheme 1. Synthesis of Substituted 1,2-Fluoroethylamines by Reaction of [Li]-(*S*)-1 with Homochiral *N*-Sulfinylimines**




With this precedent, and taking into account the difficulties associated with the preparation of homochiral fluorobenzylic centers,[17] we decided to check the synthetic potential of the new chiral monofluorinated reagent in reactions with achiral electrophiles. Michael additions of [Li]-(*S*)-**1** (Scheme 2) to activated alkenes such as α-substituted vinyl sulfones or α,β-unsaturated esters were chosen for this study because they would provide information about the ability of the stabilized monofluorocarbanion to simultaneously control the configuration of the benzylic carbon as well as that of the second chiral center created in the reaction.[18] Moreover, these reactions would expand the range of the monofluorinated compounds with the halogen atom bonded to a homochiral carbon, and in the case of reactions with

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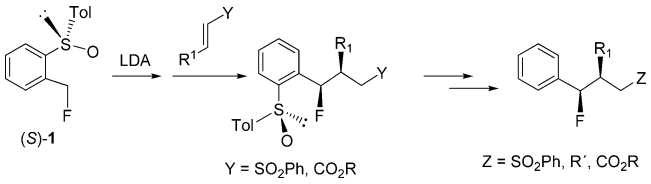
**Scheme 2. Synthesis of Homochiral Benzylic Fluorinated Centers by Reaction of (*S*)-1 with Sulfonyl and Alkoxycarbonyl Ethylenes**



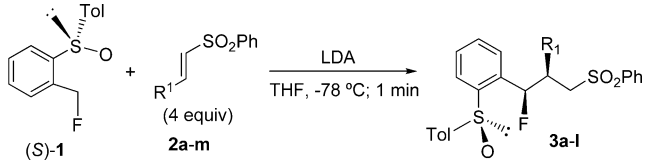

$\beta$-substituted acrylates, the ratio of 1,2- and 1,4-addition products would give some information about the hard/soft character of [Li]-(*S*)-**1**.[19]

In this paper, we describe that the *ortho*-sulfinyl group is able to get complete control of the configuration at the benzylic carbon, providing an efficient method of chiral monofluorobenzylation,[20] which makes possible the generation of enantiomerically pure benzylic fluorides by reaction of [Li]-(*S*)-**1** with $\beta$-substituted alkoxycarbonyl and sulfonyl ethylenes. The control exerted by the sulfinyl group in the configuration of the second chiral center created in these reactions is also very high, and it allows the preparation of enantiomerically pure $\gamma$-phenyl-$\gamma$-fluorinated $\beta$-substituted sulfones and esters containing two vicinal chiral centers, which had never been reported previously[21] (Scheme 2).

## RESULTS AND DISCUSSION

(*S*)-2-*p*-Tolylsulfinylbenzyl fluoride (*S*)-**1** was successfully prepared in excellent yield (88%) by nucleophilic substitution with CsF from the corresponding OTs derivative in dry acetonitrile and using [mim-*t*OH][OMs] as ionic liquid. The process is easily scalable to obtain up to 4 g of fluorinated compound (*S*)-**1**.[22] Initially, we tested its reaction with $\beta$-substituted vinyl sulfones (Table 1). The treatment of (*S*)-**1** in THF solution with lithium diisopropylamide (LDA) at −78 °C produced a instantaneous color change to deep red (suggesting the formation of [Li]-(*S*)-**1**), which quickly vanished and changed to green-blue upon addition of (*E*)-styryl phenylsulfone (**2a**) (4 equiv), affording an easily separable 92:8 mixture of diastereoisomers **3a** and **3′a**, from which the major adduct **3a** was obtained in 86% isolated yield (Table 1, entry 1). Other $\beta$-arylvinyl sulfones bearing 2-naphthyl (**2b**, entry 2, Table 1) or phenyl rings with electron-donating groups at the *para* position (**2c,d**, entries 3 and 4, Table 1) afforded similar results. Contrarily, the sulfones with electron-withdrawing groups on the benzene ring in $\beta$-position provided less homogeneous results. Thus, the presence of a fluorine atom (**2e**) has no significant influence neither in the diastereoselectivity nor in the yield (Table 1, entry 5); however, a chlorine atom (**2f**) or a cyano group (**2h**) determined important erosion in the yield, though the same high stereoselectivity remained (Table 1, entries 6 and 8). The change of behavior was more dramatic with bromo- (**2g**) and trifluoromethyl (**2i**) substituents because these reactions afforded complex mixtures where the expected adducts were not easily detected (Table 1, entries 7 and 9). These results suggest that the electronic factors play a significant role on the reactivity but are much less important on the stereoselectivity, which remains similarly high in all cases.

**Table 1. Reactions of [Li]-(*S*)-1 with $\beta$-Substituted $\alpha,\beta$-Unsaturated Phenylsulfones 2**

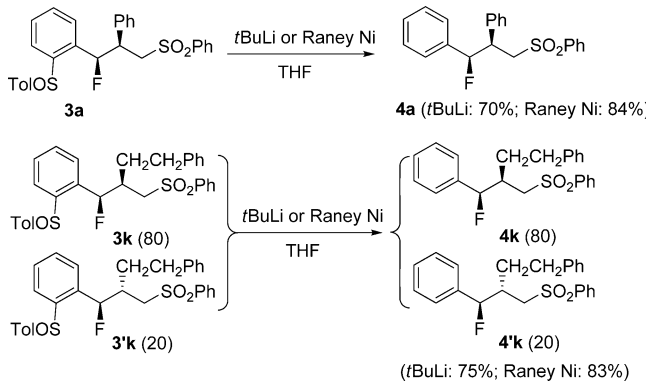



| entry[a] | sulfone | $R_1$ | dr **3**:**3′**[b] | yield (%)[c] |
|---|---|---|---|---|
| 1[d] | **2a** | $C_6H_5$ | 92:8 | 86 |
| 2 | **2b** | 2-naphthyl | 92:8 | 86 |
| 3 | **2c** | *p*-$MeOC_6H_4$ | 92:8 | 89 |
| 4 | **2d** | *p*-$MeC_6H_4$ | 92:8 | 80 |
| 5 | **2e** | *p*-$FC_6H_4$ | 92:8 | 81 |
| 6 | **2f** | *p*-$ClC_6H_4$ | 92:8 | 45[e] |
| 7 | **2g** | *p*-$BrC_6H_4$ | *f* | |
| 8 | **2h** | *p*-$CNC_6H_4$ | 92:8 | 41 |
| 9 | **2i** | *p*-$CF_3C_6H_4$ | *f* | |
| 10 | **2j** | (*E*)-$C_6H_5CH{=}CH$ | 94:6 | 70 |
| 11 | **2k** | $C_6H_5CH_2CH_2$ | 80:20 | 70[g] |
| 12 | **2l** | *n*-Pr | 76:24 | 68 |
| 13 | **2m** | *i*-Pr | *h* | |

[a]0.2 mmol of (*S*)-**1** has been used. [b]Determined by $^1$H NMR of the crude mixture. [c]Isolated yield of the major adduct after flash chromatography. [d]The reaction was also carried out with 1 mmol of (*S*)-**1**. [e]Major adduct could not be isolated as pure compound. [f]Complex mixture. [g]Isolated yield of both adducts after flash chromatography. [h]Starting material was recovered.

Removal of the chiral auxiliary from the major fluorinated sulfone adducts is interesting because it would provide compounds with two vicinal stereocenters. It can be easily performed by treatment with 3.3 equiv of *tert*-butyllithium in THF at −78 °C, as it was illustrated starting from **3a** (aryl substituted, $R_1$ = Ph) and **3k** + **3′k** (alkyl-substituted, $R_1$ = $CH_2CH_2Ph$), affording their respective desulfinylated products in 70 and 75% yields (Scheme 3). Better yields were obtained

**Scheme 3. Desulfinylation with *t*-BuLi or Raney-Ni**




using Raney-Ni as desulfinylation reagent[24] (84% from **3a** and 83% from **3k** + **3′k**). None of these procedures produces epimerization of the chiral centers present in the sulfinylated starting products, and therefore, starting from the unseparable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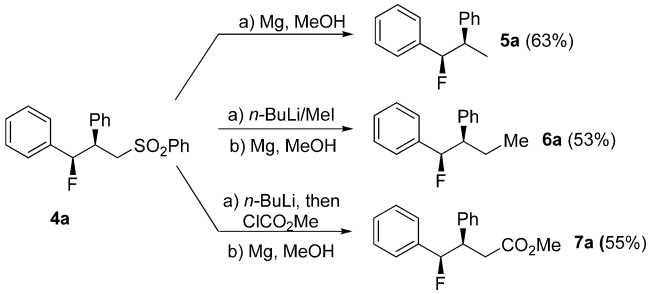
4:1 mixture of **3k** and **3′k** (Table 1, entry 11), a new 4:1 mixture of epimers, **4k** and **4′k**, was obtained, which could be separated by chromatography affording major **4k** in 65% yield. This is an interesting result to establish the relative configuration of the minor diastereoisomers obtained in Table 1 as we will see later.

The presence of the sulfone group in substrates **4** confers them an interesting reactivity that can be used for introducing different substituents before its removal (Scheme 4). This is an important task due to the difficulties inherent to the preparation of fluorinated compounds with two connected stereogenic centers in an enantiomerically pure form. Sulfone removal can be performed from **4a** with Mg/MeOH,[25] yielding **5a** in 63% yield (Scheme 4). The methylation of **4a** (*n*-BuLi and then MeI) followed by the in situ desulfonylation, yielding compound **6a** (53%), illustrates the way to perform alkylation reactions. In turn, the alkoxycarbonylation is also possible using a similar one-pot sequence with $ClCO_2Me$[26] as the electrophile (**7a**, Scheme 4).

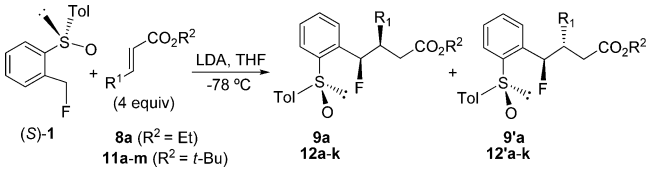
**Scheme 4. Transformations of 4a**




Configuration indicated in Table 1 for the major diastereoisomers (**3**) was established from the unequivocal assignment of **3e** performed by X-ray studies[27] (see Supporting Information), whereas that of the minor ones (**3′**) was deduced from indirect proofs. Two explanations can account for the exclusive formation of two diastereoisomers (out of the four possible ones) in the reactions of Table 1. The first one would involve the sulfinyl group completely controlling the configuration at the benzylic fluorinated carbon. Then, **3** and **3′** would be epimers in the second chiral center created in the reaction. Alternatively, the formation of a mixture of carbanions able to react in a completely stereoselective way (only yielding *syn* or *anti* products) would yield a mixture of two diastereoisomers, **3** and **3′**, now differing in the configuration of the two created chiral centers (only the configuration at the sulfur atom would be identical). Desulfinylation of the mixture **3k** + **3′k** in Scheme 3 excludes the second explanation because **4k** and **4′k** are diastereoisomers but not enantiomers. Then, we can conclude that the absolute configurations of the epimers **3** and **3′** are those indicated in Table 1 and Schemes 3 and 4.

Then we considered the direct addition of our fluorinated benzyl lithium derivative [Li]-(*S*)-**1** on $\alpha,\beta$-unsaturated esters.[28] The addition of 4 molar equiv of (*E*)-ethyl cinnamate **8a** afforded a mixture of three compounds **9a**, **9′a**, and **10a**, the two former ones (**9a** and **9′a**) being epimers at C-3[29] resulting from the conjugated addition and **10a**, the major one, the 1,2-addition product. Both an adverse regioselectivity (**9a** + **9′a**/**10a** = 30:70) and a moderate stereoselectivity (**9a**/**9′a** = 82:18) were attained (Table 2, entry 1). However, the formation of the 1,2-addition product can be avoided by using the corresponding

**Table 2. Reactions of [Li]-(*S*)-1 with $\beta$-Substituted $\alpha$, $\beta$-Unsaturated *tert*-Butyl Esters**




| entry[a] | ester | $R^1$ | products (ratio)[b] | yield (%)[c] |
|---|---|---|---|---|
| 1 | **8a** | $C_6H_5$ | **9a**/**9′a** (82:18)[d] | 20[d] |
| 2 | **11a** | $C_6H_5$ | **12a**/**12′a** (92:8) | 82 |
| 3 | **11b** | *p*-$MeOC_6H_4$ | **12b**/**12′b** (92:8) | 84[e] |
| 4 | **11c** | *p*-$MeC_6H_4$ | **12c**/**12′c** (92:8) | 85[e] |
| 5 | **11d** | *p*-$FC_6H_4$ | **12d**/**12′d** (92:8) | 89[e] |
| 6 | **11e** | *p*-$ClC_6H_4$ | **12e**/**12′e** (92:8) | 55 |
| 7 | **11f** | *p*-$BrC_6H_4$ | **12f**/**12′f** (92:8) | 38 |
| 8 | **11g** | *p*-$CNC_6H_4$ | **12g**/**12′g** (92:8) | 30[f] |
| 9 | **11h** | *p*-$CF_3C_6H_4$ | *g* | |
| 10 | **11i** | (*E*)-$C_6H_5CH{=}CH$ | **12i**/**12′i** (>98:<2) | 76 |
| 11 | **11j** | *n*-Pr | **12j**/**12′j** (>98:<2) | 77 |
| 12 | **11k** | $C_6H_5CH_2CH_2$ | **12k**/**12′k** (>98:<2) | 79 |
| 13 | **11l** | Bn | no reaction | |
| 14 | **11m** | *i*Pr | no reaction | |

[a]0.2 mmol of (*S*)-**1** has been used. [b]Determined by $^1H$ NMR of the crude mixture. [c]Isolated yields of the major isomer after flash chromatography. [d]**10a** was obtained as major compound (see text). [e]Combined yield. [f]Major adduct could not be isolated as pure compound. [g]Complex mixture.

*tert*-butyl ester **11a** as electrophilic partner, which allows the complete regiocontrol, only yielding the Michael products **12a** and **12′a**, and a substantial increase of the stereoselectivity (92:8) (Table 2, compare entries 1 and 2).

Then we investigated the scope of the reaction with other unsaturated aromatic *tert*-butyl esters containing electron-withdrawing and electron-donating groups on the aromatic ring (**11b**–**g**). All of them evolved into 92:8 mixtures of the 1,4-adducts **12** and **12′**, regardless of the electronic character of the substituents at the phenyl ring (Table 2, entries 3–8). As in the case of sulfones, the lowest yields are obtained with electron-withdrawing groups (**11e**–**11g**, entries 6–8). Separation of the mixtures could be performed only in the later cases, which allowed the isolation of the major isomers (**12e** and **12f**) with higher than 98% de. The *p*-trifluoromethylphenyl derivative **11h** afforded a complex mixture where the conjugate addition products could not be detected (Table 2, entry 9). The reactions with alkenyl (**11i**) and alkyl-substituted (**11j** and **11k**) acrylates evolved with a complete control of the stereoselectivity, only yielding one diastereoisomer (**12i**–**k**, Table 2, entries 10–12). The failure of the reaction of **11l** ($R_1$ = Bn) and **11m** ($R_1$ = *i*-Pr) is noteworthy. The easy deprotonation of **11l** and the steric hindrance of **11m** could be responsible for their lack of reactivity.

Desulfinylation of the resulting compounds can be successfully performed with Raney-Ni[30] under similar conditions to that used with the sulfones in Scheme 3 to afford the corresponding *tert*-butyl butanoates (Table 3) without affecting the enantiomeric integrity. This protocol was applied to obtain compounds **13b**, **13c**, **13d** ($R_1$ aromatic), and **13k** ($R_1$ aliphatic). In the three former cases, we used as starting compounds the unseparable 92:8 diastereomeric mixtures in Table 2, which afforded 92:8 mixtures of their corresponding **13** and **13′**, which could now be separated. Thus, reactions of (*S*)-**1** with $\beta$-substituted acrylates


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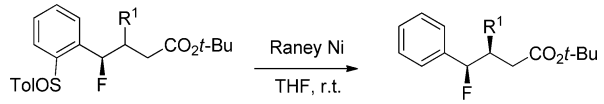
**Table 3. Synthesis of Enantiomerically Pure β-Substituted γ-Fluoroesters (13) by Desulfinylation of Their Precursors**




12+12′ 13

| entry | starting ester | $R^1$ | compound (%)[a] |
|---|---|---|---|
| 1 | **12b** + **12′b** | *p*-$MeOC_6H_4$ | **13b** (85) |
| 2 | **12c** + **12′c** | *p*-$MeC_6H_4$ | **13c** (87) |
| 3 | **12d** + **12′d** | *p*-$FC_6H_4$ | **13d** (86) |
| 4 | **12k** | $C_6H_5CH_2CH_2$ | **13k** (80) |

[a]Isolated yield of the major epimer after flash chromatography.

followed by desulfinylation gave access to β-substituted γ-fluoroesters bearing two connected chiral centers in only two steps, with good yields and excellent diastereoselectivities.

The formation of the major isomers **12** could be explained by assuming the approach depicted in Scheme 5. The carbanion, stabilized by hydrogen bonds with the N−H of the amine,[31] only has one accessible face for attacking the electrophile. It would explain the *R* configuration observed for compounds **3** (and **3′**) and **12** (and **12′**) obtained, respectively, from vinyl sulfones and acrylates. The *R* or *S* configuration at the second chiral center depends on the electrophile's face being attacked by the carbanion. Approaches A and B (Scheme 5) are those resulting from the presumably favored orientations of the electrophilic double bond (with an antiperiplanar arrangement with respect to the aromatic ring bonded to the carbanion). Major compounds (**3** and **12**) result from the approach A, which suggests that the $(SOTol\text{-}Ar/R)_{gauche}$ is larger than $[(Ar/R)_{gauche} + (R/F)_{gauche}]$ destabilizing B.

## CONCLUSION

We have demonstrated that monofluorobenzylcarbanions stabilized by a remote homochiral sulfinyl group react with high stereoselectivity and good yields with β-aryl-substituted vinyl aryl sulfones (92:8 dr) if the aryl substituent bears electron-donating groups or F in *para* position. The obtained sulfonyl adducts could be transformed successfully, by successive desulfinylation and desulfonylation reactions (with or without previous alkylation) and without loss of configurational integrity in the corresponding 1,2-diarylfluoroalkanes. On the other hand, the same monofluorobenzyl lithium derivatives afforded the corresponding Michael adducts, with high or complete diastereoselectivity by addition to β-aryl or β-alkyl α,β-unsaturated *tert*-butyl esters, respectively. However, with the β-aryl esters, although the ring substituent effect is not related to the diastereoselectivity, a strong decrease in yield (*p*-Cl, *p*-Br, or *p*-CN) or no adduct (*p*-$CF_3$) is observed with electron-withdrawing groups bonded to the aromatic ring. The importance of the Michael-type process described herein, which takes place with high yields and excellent stereoselectivities, lies in the preparation of enantiomerically pure fluorinated compounds that, to the best of our knowledge, have not been prepared so far.

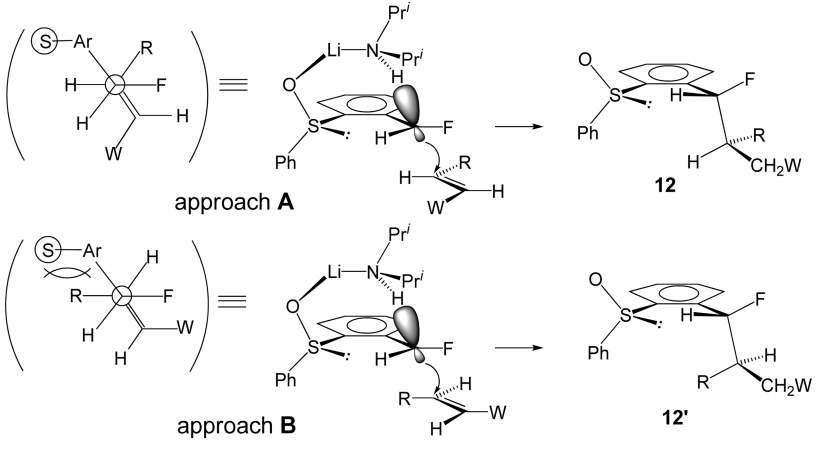
## EXPERIMENTAL SECTION

**General Procedures.** $^1H$ NMR spectra were acquired at 300 MHz, and $^{13}C$ NMR spectra were acquired at 75 MHz. $^{19}F$ NMR spectra were acquired at 282.4 MHz. Chemical shifts (δ) are reported in parts per million relative to residual solvent signals ($CHCl_3$, 7.26 ppm for $^1H$ NMR, $CDCl_3$, 77.0 ppm for $^{13}C$ NMR spectra). $^{13}C$ NMR spectra were acquired on a broad-band proton decoupled mode. High-resolution mass spectra (HRMS) were obtained with an electrospray ion source. Melting points were determined in open capillary tubes. All reactions were carried out in anhydrous solvents and under an argon atmosphere. Commercial anhydrous THF was dried with molecular sieves. $iPr_2NH$ was distilled from KOH. Analytical thin layer chromatography (TLC) was performed using precoated aluminum-backed plates (Kieselgel 60 F254) and visualized by ultraviolet irradiation or $KMnO_4$ dip. Flash column chromatography was performed by using silica gel (230−400 mesh).

Commercially available starting materials and solvents were used without purification. Compound (*S*)-**1**[15] was previously synthesized, and vinyl sulfones and unsaturated esters were obtained according to the literature.[32]

**General Procedure for the Conjugate Addition of Sulfoxide (*S*)-1 to Vinyl Sulfones and α,β-Unsaturated Esters.** A solution of *n*-BuLi (0.24 mmol, 2.5 M in hexane) was added over $iPr_2NH$ (0.36 mmol) in THF (1.2 mL) at 0 °C. After stirring for 10 min, the mixture was cooled at −78 °C and then a solution of (*S*)-**1** (0.20 mmol) in THF (1 mL) was added. After stirring for 5 min, the corresponding vinyl sulfones **2a−m** (Table 1) or unsaturated ester **11a−m** (Table 2) (0.8 mmol) in THF (0.4 mL) were added at −78 °C. Immediately, the reaction mixture was hydrolyzed (2 mL of saturated $NH_4Cl$), extracted (3 × 10 mL $Et_2O$), washed (2 × 10 mL of saturated NaCl), dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residue was purified by flash column chromatography. The eluent and

**Scheme 5. Favored Approaches of β-Substituted Vinyl Sulfones or α,β-Unsaturated Esters to the Only Accessible Face of the Carbanionic Species**





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the obtained yield in each case are indicated below or in the Supporting Information.

**(2*R*,3*R*)-3-Fluoro-3-{2-[(*S*)-*p*-tolylsulfinyl]phenyl}-2-phenylprop-1-yl phenyl sulfone (3a).** Compound **3a** was obtained as the major diastereomer from vinyl sulfone **2a** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 3:1; yield 86%; colorless oil; $[\alpha]^{20}_D$ 64 (*c* 0.5, $CHCl_3$); IR (NaCl) 2965, 2922, 1447, 1305, 1141, 1085 $cm^{-1}$; $^1H$ NMR $\delta$ 7.95 (d, *J* = 7.9 Hz, 1H), 7.59−7.45 (m, 6H), 7.36−7.28 (m, 6H), 7.14−7.02 (m, 3H), 6.97−6.94 (m, 1H), 6.78 (d, *J* = 7.9 Hz, 1H), 6.32 (dd, $^2J_{H-F}$ = 45.8 and *J* = 4.6 Hz, 1H), 3.67−3.44 (m, 3H), 2.38 (s, 3H); $^{13}C$ NMR $\delta$ 142.3, 142.2, 142.0, 141.4, 139.6, 136.3, 136.1, 135.5, 133.3, 131.2. 130.3, 129.5, 129.2, 129.0, 128.2, 128.0, 127.9, 127.8, 127.7, 127.5, 126.0, 91.1 (d, $^1J_{C-F}$ = 176.3 Hz), 58.0 (d, $^3J_{C-F}$ = 4.5 Hz), 46.6 (d, $^2J_{C-F}$ = 23.2 Hz), 21.4; $^{19}F$ NMR $\delta$ −180.8; MS (ESI+) *m*/*z* (%) 493 $[M + H]^+$ (100), 515 $[M + Na]^+$ (21), 473 $[M - F]^+$ (33); HRMS *m*/*z* calcd for $C_{28}H_{26}O_3FS_2$ 493.1301, found 493.1299.

**(2*R*,3*R*)-3-Fluoro-3-{2-[(*S*)-*p*-tolylsulfinyl]phenyl}-2(1-naphthyl)prop-1-yl phenyl sulfone (3b).** Compound **3b** was obtained as the major diastereomer from vinyl sulfone **2b** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 3:1; yield 86%; colorless oil; $[\alpha]^{20}_D$ 154 (*c* 1.0, $CHCl_3$); $^1H$ NMR $\delta$ 7.87 (d, *J* = 7.8 Hz, 1H), 7.63−7.60 (m, 1H), 7.47−7.32 (m, 9H), 7.5−7.11 (m, 5H), 7.02 (d, *J* = 7.7 Hz, 2H), 6.98−6.93 (m, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.32 (dd, $^2J_{H-F}$ = 45.9 and *J* = 4.7 Hz, 1H), 3.74−3.40 (m, 3H), 2.32 (s, 3H); $^{13}C$ NMR $\delta$ 142.1, 141.3, 139.5, 136.5, 136.4, 133.0, 132.9, 132.9, 132.7,131.4, 130.4, 129.5, 128.8, 128.6, 128.2, 128.1, 128.0, 127.7, 127.6, 127.5, 126.3, 126.3, 126.1, 126.0, 90.9 (d, $^1J_{C-F}$ = 179.2 Hz), 58.2 (d, $^3J_{C-F}$ = 4.5 Hz), 46.9 (d, $^2J_{C-F}$ = 24.3 Hz), 21.4; $^{19}F$ NMR $\delta$ −179.6; IR (NaCl) 2923, 1509, 1305, 1216, 1138, 1084 $cm^{-1}$; MS (ESI+) *m*/*z* (%) 565 $[M + Na]^+$ (18), 543 $[M + 1]^+$ (100), 523 $[M - F]^+$ (26); HRMS *m*/*z* calcd for $C_{32}H_{28}O_3FS_2$ 543.1456, found 543.1458.

**(2*R*,3*R*)-3-Fluoro-3-{2-[(*S*)-*p*-tolylsulfinyl]phenyl}-2-(4-methoxyphenyl)prop-1-yl phenyl sulfone (3c).** Compound **3c** was obtained as the major diastereomer from vinyl sulfone **2c** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 3:1; yield 89%; colorless oil; $[\alpha]^{20}_D$ 66 (*c* 1.0, $CHCl_3$); $^1H$ NMR $\delta$ 7.94 (d, *J* = 7.9 Hz, 1H), 7.61−7.44 (m, 6H), 7.36−7.26 (m, 5H), 6.94 (d, *J* = 8.8 Hz, 1H), 6.68 (d, *J* = 8.5 Hz, 2H), 6.56 (d, *J* = 8.8 Hz, 2H), 6.27 (dd, $^2J_{H-F}$ = 45.8 and *J* = 4.5 Hz, 1H), 3.71 (s, 3H), 3.67−3.36 (m, 3H), 2.38 (s, 3H); $^{13}C$ NMR $\delta$ 159.0, 142.1, 142.1, 142.0, 141.4, 139.8, 136.5, 136.2, 133.2, 131.1, 130.3, 130.2, 129.4, 128.9, 128.0, 127.9, 127.8, 127.3, 125.9, 113.7, 91.4 (d, $^1J_{C-F}$ = 176.3 Hz), 58.3 (d, $^3J_{C-F}$ = 4.0 Hz), 55.2, 45.9 (d, $^2J_{C-F}$ = 23.8 Hz), 21.4; $^{19}F$ NMR $\delta$ −181.1; IR (NaCl) 3020, 2895, 1515, 1305, 1216, 1035 $cm^{-1}$; MS (ESI+) *m*/*z* (%) 545 $[M + Na]^+$ (18), 523 $[M + 1]^+$ (100), 503 $[M - F]^+$ (36); HRMS *m*/*z* calcd for $C_{29}H_{28}O_4FS_2$ 523.1407, found 523.1413.

**(2*R*,3*R*)-3-Fluoro-3-{2-[(*S*)-*p*-tolylsulfinyl]phenyl}-2-(4-tolyl)-prop-1-yl phenyl sulfone (3d).** Compound **3d** was obtained as the major diastereomer from vinyl sulfone **2d** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 3:1; yield 80%; colorless oil; $[\alpha]^{20}_D$ 77 (*c* 1.0, $CHCl_3$); $^1H$ NMR $\delta$ 7.94 (d, *J* = 7.6 Hz, 1H), 7.58−7.44 (m, 6H), 7.35−7.27 (m, 5H), 6.99 (dd, *J* = 7.8, 1.3 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 2H), 6.68 (d, *J* = 7.8 Hz, 2H), 6.29 (dd, $^2J_{H-F}$ = 45.8 and *J* = 4.7 Hz, 1H), 3.64−3.39 (m, 3H), 2.37 (s, 3H), 2.23 (s, 3H); $^{13}C$ NMR $\delta$ 142.3, 142.2, 142.0, 141.4, 139.7, 137.3, 136.5, 136.2, 133.1, 132.4, 131.2, 130.3, 129.5, 129.0, 128.9, 128.9, 128.0, 127.9, 127.8, 125.9, 91.2 (d, $^1J_{C-F}$ = 179.3 Hz), 58.5 (d, $^3J_{C-F}$ = 4.3 Hz), 46.3 (d, $^2J_{C-F}$ = 24.2 Hz), 21.4, 21.0; $^{19}F$ NMR $\delta$ −180.2; IR (NaCl) 3021, 2923, 1515, 1306, 1141, 1084 $cm^{-1}$; MS (ESI+) *m*/*z* (%) 529 $[M + Na]^+$ (33), 507 $[M + 1]^+$ (100), 487 $[M - F]^+$ (50); HRMS *m*/*z* calcd for $C_{29}H_{28}O_3FS_2$ 507.1458, found 507.1459.

**(2*R*,3*R*)-3-Fluoro-3-{2-[(*S*)-*p*-tolylsulfinyl]phenyl}-2-(4-fluorophenyl)prop-1-yl phenyl sulfone (3e).** Compound **3e** was obtained as the major diastereomer from vinyl sulfone **2e** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 3:1; yield 81%; white solid; mp 131−133 °C; $[\alpha]^{20}_D$ 102 (*c* 0.9, $CHCl_3$); $^1H$ NMR $\delta$ 7.93 (d, *J* = 7.8 Hz, 1H), 7.58−7.46 (m, 6H), 7.38−7.28 (m, 5H), 6.96 (d, *J* = 7.8 Hz, 1H), 6.77−6.73 (m, 4H), 6.27 (dd, $^2J_{H-F}$ = 45.9 and *J* = 4.6 Hz, 1H), 3.72−3.39 (m, 3H), 2.38 (s, 3H); $^{13}C$ NMR $\delta$ 162.2 (d, $^1J_{C-F}$ = 247.0 Hz), 142.0, 142.0, 141.9, 139.6, 136.4, 136.1, 133.3, 131.3, 131.3 (d, $^4J_{C-F}$ = 3.4 Hz), 130.7 (d, $^3J_{C-F}$ = 8.0 Hz), 130.3, 129.5, 128.0 (d, $^3J_{C-F}$ = 8.1 Hz), 127.7, 126.4, 125.7, 126.4, 125.7, 115.1 (d, $^2J_{C-F}$ = 21.4 Hz), 91.1 (d, $^1J_{C-F}$ = 179.7 Hz), 58.2 (d, $^3J_{C-F}$ = 4.3 Hz), 46.1 (d, $^3J_{C-F}$ = 23.9 Hz), 21.4; $^{19}F$ NMR $\delta$ −114.4, −181.5; IR (KBr) 2975, 2921, 1511, 1307, 1140, 1084 $cm^{-1}$; MS (ESI+) *m*/*z* (%) 533 $[M + Na]^+$ (35), 511 $[M + 1]^+$ (100), 491 $[M - F]^+$ (40); HRMS *m*/*z* calcd for $C_{28}H_{25}O_3F_2S_2$ 511.1207, found 511.1204.

**(2*R*,3*R*)-3-Fluoro-3-{2-[(*S*)-*p*-tolylsulfinyl]phenyl}-2-(4-cyanophenyl)prop-1-yl phenyl sulfone (3h).** Compound **3h** was obtained as the major diastereomer from vinyl sulfone **2h** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 3:1; yield 41%; colorless oil; $[\alpha]^{20}_D$ 114 (*c* 1.1, $CHCl_3$); $^1H$ NMR $\delta$ 7.87 (d, *J* = 7.9 Hz, 1H), 7.56−7.46 (m, 5H), 7.43−7.33 (m, 8H), 7.28−7.26 (m, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.28 (dd, $^2J_{H-F}$ = 46.0 and *J* = 4.9 Hz, 1H), 3.76−3.62 (m, 2H), 3.37−3.33 (m, 1H), 2.36 (s, 3H); $^{13}C$ NMR $\delta$ 142.0, 141.8, 141.6, 140.8, 139.4, 136.4, 136.1, 133.5, 131.9, 131.8, 130.3, 130.0, 129.7, 129.1, 128.0, 127.9, 127.7, 127.2, 125.3, 118.4 (C≡N), 111.6, 90.7 (d, $^1J_{C-F}$ = 179.9 Hz), 57.8 (d, $^3J_{C-F}$ = 4.5 Hz), 47.0 (d, $^2J_{C-F}$ = 24.4 Hz), 21.4; $^{19}F$ NMR $\delta$ −180.7; IR (NaCl) 2985, 2925, 2229, 1447, 1306, 1142, 1084 $cm^{-1}$; MS (ESI+) *m*/*z* (%) 540 $[M + Na]^+$ (33), 518 $[M + 1]^+$ (100), 498 $[M - F]^+$ (34); HRMS *m*/*z* calcd for $C_{29}H_{25}NO_3FS_2$ 518.1249, found 518.1254.

**(2*R*,3*E*)-2-((*R*)-Fluoro{2-[(*S*)-*p*-tolylsulfinyl]phenyl}methyl)-4-phenylbut-3-en-1-yl phenyl sulfone (3j).** Compound **3j** was obtained as the major diastereomer from vinyl sulfone **2j** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 3:1; yield 70%; colorless oil; $[\alpha]^{20}_D$ 56 (*c* 1.6, $CHCl_3$); $^1H$ NMR $\delta$ 7.96 (d, *J* = 7.6 Hz, 1H), 7.83−7.81 (m, 2H), 7.56−7.4 (m, 8H), 7.29−7.21 (m, 5H), 7.10−7.07 (m, 2H), 6.27 (dd, $^2J_{H-F}$ = 45.8 and *J* = 4.5 Hz, 1H), 5.94−5.76 (m, 2H), 3.42−3.30 (m, 2H), 3.24−3.08 (m, 1H), 2.39 (s, 3H); $^{13}C$ NMR $\delta$ 142.2, 142.2, 141.9, 141.5, 139.7, 136.4, 136.1, 136.1, 135.6, 133.6, 131.1, 130.2, 129.6, 129.2, 128.4, 128.4, 128.1, 128.0, 127.9, 126.4, 126.2, 125.9, 123.2, 123.1, 91.4 (d, $^1J_{C-F}$ = 179.3 Hz), 57.6 (d, $^3J_{C-F}$ = 3.2 Hz), 44.8 (d, $^2J_{C-F}$ = 23.4 Hz), 21.4; $^{19}F$ NMR $\delta$ −183.2; IR (NaCl): 3035, 2924, 1493, 1306, 1216, 1084 $cm^{-1}$; MS (ESI+) *m*/*z* (%) 541 $[M + Na]^+$ (23), 519 $[M + 1]^+$ (100), 499 $[M - F]^+$ (36); HRMS *m*/*z* calcd for $C_{30}H_{28}O_3FS_2$ 519.1448, found 519.1458.

**(2*R*)-2-((*R*)-Fluoro{2-[(*S*)-*p*-tolylsulfinyl]phenyl}methyl)-4-phenylbutyl phenyl sulfone (3k).** Compound **3k** was obtained as the major diastereomer from vinyl sulfone **2k** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 3:1; yield 70%; colorless oil; $[\alpha]^{20}_D$ −35 (*c* 1.5, $CHCl_3$); $^1H$ NMR $\delta$ 8.03 (d, *J* = 7.8 Hz, 1H), 7.82−7.74 (m, 2H), 7.68−7.61 (m, 1H), 7.57−7.39 (m, 7H), 7.25−7.15 (m, 5H), 7.02−6.94 (m, 2H), 6.14 (dd, $^2J_{H-F}$ = 46.1 and *J* = 5.5 Hz, 1H), 3.12−2.92 (m, 2H), 2.60−2.51 (m, 2H), 2.37−2.33 (m, 1H), 2.36 (s, 3H), 1.95−1.89 (m, 2H); $^{13}C$ NMR $\delta$ 143.1, 141.8, 141.7, 140.9, 139.5, 136.3, 136.0, 133.8, 131.4, 130.1, 129.7, 129.4, 128.5, 128.4, 127.7, 127.3, 127.2, 126.1, 126.1, 125.9, 92.3 (d, $^1J_{C-F}$ = 178.0 Hz), 55.7 (d, $^3J_{C-F}$ = 4.8 Hz), 39.1 (d, $^2J_{C-F}$ = 24.4 Hz), 32.4, 30.0, 21.4; $^{19}F$ NMR $\delta$ −181.4; IR (NaCl) 3035, 2925, 2229, 1494, 1307, 1148, 1085 $cm^{-1}$; MS (ESI+) *m*/*z* (%) 543 $[M + Na]^+$ (19), 521 $[M + H]^+$ (100), 501 $[M - F]^+$ (63); HRMS *m*/*z* calcd for $C_{30}H_{30}O_3FS_2$ 521.1614, found 521.1622.

**(2*R*)-2((*R*)-Fluoro{2-[(*S*)-*p*-tolylsulfinyl]phenyl}methyl)pentyl phenyl sulfone (3l + 3l′).** This compound was obtained as a 88:12 (**3l** + **3l′**) enriched mixture from vinyl sulfone **2l** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 3:1; yield 68%; colorless oil; $[\alpha]^{20}_D$ −41 (*c* 1.9, $CHCl_3$); $^1H$ NMR $\delta$ 8.05 (d, *J* = 6.7 Hz, 1H), 7.84−7.81 (m, 2H), 7.55−7.44 (m, 7H), 7.38−7.33 (m, 1H), 7.22 (d, *J* = 8.2 Hz, 2H), 6.14 (dd, $^2J_{H-F}$ = 46.0 and *J* = 5.2 Hz, 1H, A), 5.76 (dd, $^2J_{H-F}$ = 46.0 and *J* = 4.9 Hz, B), 3.07 (dd, *J* = 14.7, 6.4 Hz, 1H), 2.92 (dd, *J* = 14.7, 5.2 Hz, 1H), 2.55−2.39 (m, 1H), 2.34 (s, 3H), 1.63−1.39 (m, 2H), 1.33−1.22 (m, 1H), 0.89−0.75 (m, 1H), 0.72 (t, *J* = 7.2 Hz, 3H); $^{13}C$ NMR $\delta$ 143.1, 141.9, 141.7, 139.7, 136.3, 136.0, 133.8, 131.3, 130.2, 130.0, 129.7, 129.4, 127.8, 127.3, 127.1, 125.9, 125.9, 125.9, 92.3 (d, $^1J_{C-F}$ = 178.1 Hz), 55.3 (d, $^3J_{C-F}$ = 4.7 Hz), 39.3 (d, $^2J_{C-F}$ = 23.7 Hz), 29.8, 21.4, 19.2, 13.8; $^{19}F$ NMR $\delta$ −182.6 (A), −186.82 (B); IR (NaCl) 2961, 2873, 2229, 1447, 1307, 1148, 1084 $cm^{-1}$; MS (ESI+) *m*/*z* (%)


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481 [M + Na]$^+$ (100), 459 [M + 1]$^+$ (73), 439 [M − F]$^+$ (55); HRMS $m/z$ calcd for $C_{25}H_{28}O_3FS_2$ 459.1458, found 459.1441.

***tert*-Butyl (3*R*,4*R*)-4-Fluoro-{2-[(*S*)-*p*-tolylsulfinyl]phenyl}-3-phenylbutanoate (12a).** Compound **12a** was obtained as the major diastereomer from unsaturated ester **11a** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 2:1; yield 82%; colorless oil; $[\alpha]^{20}_D$ 24 ($c$ 1.5, $CHCl_3$); $^1$H NMR $\delta$ 8.00 (d, $J$ = 7.9 Hz, 1H), 7.55 (d, $J$ = 8.2 Hz, 2H), 7.50−7.45 (m, 1H), 7.34−7.28 (m, 2H), 7.23−7.17 (m, 4H), 7.01−6.97 (m, 3H), 6.11 (dd, $^2J_{H\text{-}F}$ = 46.0 and $J$ = 5.3 Hz, 1H), 3.41−3.26 (m, 1H), 2.68−2.52 (m, 2H), 2.37 (s, 3H), 1.22 (s, 9H); $^{13}$C NMR $\delta$ 170.3, 142.7, 142.6, 141.9, 141.8, 137.7, 136.9, 136.6, 130.8, 130.1, 129.8, 129.4, 129.1, 128.1, 128.0, 127.9, 127.3, 126.1, 125.6, 92.5 (d, $^1J_{C\text{-}F}$ = 178.7 Hz), 80.6, 47.8 (d, $^2J_{C\text{-}F}$ = 22.7 Hz), 38.0 (d, $^3J_{C\text{-}F}$ = 4.5 Hz), 27.8, 21.4; $^{19}$F NMR $\delta$ −178.1; IR (NaCl) 2978, 2868, 2229, 1727, 1393, 1258, 1150 cm$^{-1}$; MS (ESI+) $m/z$ (%) 927 [2M + Na]$^+$ (43), 475 [M + Na]$^+$ (100), 453 [M + H]$^+$ (42), 397 (66); HRMS $m/z$ calcd for $C_{27}H_{30}O_3FS$ 453.1876, found 453.1894.

***tert*-Butyl (3*R*,4*R*)-4-Fluoro-4-{2-[(*S*)-*p*-tolylsulfinyl]phenyl}-3-(4-chlorophenyl)butanoate (12e).** Compound **12e** was obtained as the major diastereomer from unsaturated ester **11e** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 3:1; yield 55%; colorless oil; $[\alpha]^{20}_D$ 17 ($c$ 1.4, $CHCl_3$); $^1$H NMR $\delta$ 7.98 (d, $J$ = 8.0 Hz, 1H), 7.53−7.46 (m, 3H), 7.36−7.32 (m, 3H), 7.21−7.18 (m, 2H), 6.99−6.92 (m, 3H), 6.10 (dd, $^2J_{H\text{-}F}$ = 46.1 and $J$ = 5.2 Hz, 1H), 3.39−3.24 (m, 1H), 2.69−2.51 (m, 2H), 2.37 (s, 3H), 1.24 (s, 9H); $^{13}$C NMR $\delta$ 170.0, 142.4, 142.4, 141.9, 141.7, 136.8, 136.6, 136.3, 133.1, 131.0, 130.5, 130.1, 129.9, 129.5, 128.2, 128.0, 127.9, 127.7, 125.9, 92.0 (d, $^1J_{C\text{-}F}$ = 178.6 Hz), 80.8, 47.3 (d, $^2J_{C\text{-}F}$ = 22.9 Hz), 38.0 (d, $^3J_{C\text{-}F}$ = 4.1 Hz), 27.8, 21.4; $^{19}$F NMR $\delta$ −178.9; IR (NaCl) 2985, 2896, 2229, 1733, 1503, 1383, 1253 cm$^{-1}$; MS (ESI+) $m/z$ (%) 509 [M + Na]$^+$ (23), 487 [M + 1]$^+$ (63), 431 (100); HRMS $m/z$ calcd for $C_{27}H_{29}O_3FSCl$ 487.1504, found 487.1518.

***tert*-Butyl (3*R*,4*R*)-4-Fluoro-4-{2-[(*S*)-*p*-tolylsulfinyl]phenyl}-3-(4-bromophenyl)butanoate (12f).** Compound **12f** was obtained as the major diastereomer from unsaturated ester **11f** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 2:1; yield 38%; colorless oil; $[\alpha]^{20}_D$ 31 ($c$ 1.6, $CHCl_3$); $^1$H NMR $\delta$ 8.06−7.86 (m, 1H), 7.53−7.50 (m, 3H), 7.37−7.30 (m, 3H), 7.29−7.27 (m, 2H), 7.00−6.97 (m, 1H), 6.88 (d, $J$ = 8.3 Hz, 2H), 6.10 (dd, $^2J_{H\text{-}F}$ = 46.0 and $J$ = 5.2 Hz, 1H), 3.39−3.23 (m, 1H), 2.66−2.52 (m, 2H), 2.37 (s, 3H), 1.24 (s, 9H); $^{13}$C NMR $\delta$ 170.0, 142.4, 142.4, 142.1, 141.9, 141.6, 136.9, 136.9, 136.6, 131.2, 131.0, 130.8, 130.1, 129.5, 128.0, 127.9, 126.5, 125.9, 121.2, 91.9 (d, $^1J_{C\text{-}F}$ = 178.6 Hz), 80.8, 47.3 (d, $^2J_{C\text{-}F}$ = 22.7 Hz), 37.9 (d, $^3J_{C\text{-}F}$ = 4.1 Hz), 27.8, 21.4; $^{19}$F NMR $\delta$ −178.8; IR (NaCl) 2978, 2915, 2229, 1727, 1492, 1365, 1258 cm$^{-1}$; MS (ESI+) $m/z$ (%) 533 [M + 2]$^+$ (57), 397 [M]$^+$ (52), 477 (100); HRMS $m/z$ calcd for $C_{27}H_{29}O_3FSBr$ 531.1006, found 531.0999.

***tert*-Butyl (3*R*,4*E*)-3-((*R*)-Fluoro{2-[(*S*)-*p*-tolylsulfinyl]phenyl}-methyl)-5-phenylpent-4-enoate (12i).** Compound **12i** was obtained as a unique diastereomer from unsaturated ester **11i** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 2:1; yield 76%; colorless oil; $[\alpha]^{20}_D$ 33 ($c$ 1.0, $CHCl_3$); $^1$H NMR $\delta$ 8.04−7.99 (m, 1H), 7.53−7.37 (m, 6H), 7.27−7.19 (m, 6H), 6.15−6.13 (m, 2H), 6.00 (dd, $^2J_{H\text{-}F}$ = 46.2 and $J$ = 4.8 Hz, 1H), 3.10−2.95 (m, 1H), 2.49−2.31 (m, 2H), 2.36 (s, 3H), 1.24 (s, 9H); $^{13}$C NMR $\delta$ 170.5, 142.8, 141.9, 141.7, 137.1, 136.8, 136.8, 134.0, 131.0, 130.0, 129.6, 128.5, 127.9, 127.7, 127.6, 126.3, 126.0, 126.0, 125.9, 125.6, 125.6, 92.7 (d, $^1J_{C\text{-}F}$ = 177.8 Hz), 80.8, 45.9 (d, $^2J_{C\text{-}F}$ = 22.8 Hz), 37.8 (d, $^3J_{C\text{-}F}$ = 3.5 Hz), 28.1, 21.4; $^{19}$F NMR $\delta$ −178.9; IR (NaCl) 2980, 2806, 1726, 1493, 1368, 1151 cm$^{-1}$; MS (ESI+) $m/z$ (%) 501 [M + Na]$^+$ (52), 479 [M + H]$^+$ (53), 423 (100); HRMS $m/z$ calcd for $C_{29}H_{32}O_3FS$ 479.2050, found 479.2067.

***tert*-Butyl (3*S*)-3-((*R*)-Fluoro{2-[(*S*)-*p*-tolylsulfinyl]phenyl}-methyl)hexanoate (12j).** Compound **12j** was obtained as a unique diastereomer from unsaturated ester **11j** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 2:1; yield 77%; colorless oil; $[\alpha]^{20}_D$ −68 ($c$ 0.5, $CHCl_3$); $^1$H NMR $\delta$ 8.05 (d, $J$ = 6.9 Hz, 1H), 7.53−7.39 (m, 5H), 7.23 (d, $J$ = 8.1 Hz, 2H), 5.85 (dd, $^2J_{H\text{-}F}$ = 46.6 and $J$ = 6.4 Hz, 1H), 2.52−2.38 (m, 1H), 2.35 (s, 3H), 2.10 (dc, $J$ = 15.6, 6.5 Hz, 2H), 1.58−1.47 (m, 3H), 1.41 (s, 9H), 1.23−1.10 (m, 1H), 0.85 (d, $J$ = 7.2 Hz, 3H); $^{13}$C NMR $\delta$ 171.4, 143.7, 142.4, 141.4, 137.3, 137.0, 131.0, 129.9, 129.6, 127.7, 127.6, 125.9, 125.9, 94.5 (d, $^1J_{C\text{-}F}$ = 175.6 Hz), 80.7, 40.7 (d, $^2J_{C\text{-}F}$ = 22.7 Hz), 36.0 (d, $^3J_{C\text{-}F}$ = 5.1 Hz), 30.8 (d, $^3J_{C\text{-}F}$ = 2.9 Hz), 28.1, 21.3, 19.8, 14.1; $^{19}$F NMR $\delta$ −177.2; IR (NaCl) 2962, 2873, 1726, 1493, 1393, 1154 cm$^{-1}$; MS (ESI+) $m/z$ (%) 859 [2M + Na]$^+$ (34), 441 [M + Na]$^+$ (100), 419 [M + H]$^+$ (33); HRMS $m/z$ calcd for $C_{24}H_{32}O_3FS$ 419.2050, found 419.2035.

***tert*-Butyl (3*S*)-3-((*R*)-Fluoro{2-[(*S*)-*p*-tolylsulfinyl]phenyl}-methyl)-5-phenylpentanoate (12k).** Compound **12k** was obtained as a unique diastereomer from unsaturated ester **11k** and (*S*)-**1**. Chromatography: *n*-hexane/AcOEt, 2:1; yield 79%; colorless oil; $[\alpha]^{20}_D$ −43 ($c$ 0.5, $CHCl_3$); $^1$H NMR $\delta$ 8.04 (d, $J$ = 7.6 Hz, 1H), 7.55−7.47 (m, 4H), 7.45−7.39 (m, 1H), 7.28−7.19 (m, 5H), 7.12−7.10 (m, 2H), 5.91 (dd, $^2J_{H\text{-}F}$ = 46.5 and $J$ = 6.5 Hz, 1H), 2.75−2.65 (m, 1H), 2.59−2.43 (m, 2H), 2.36 (s, 3H), 2.28−2.11 (m, 2H), 2.01−1.89 (m, 1H), 1.84−1.76 (m, 1H), 1.43 (s, 9H); $^{13}$C NMR $\delta$ 171.2, 143.6, 142.2, 141.8, 141.4, 137.2, 136.9, 131.1, 129.9, 129.7, 129.7, 128.4, 128.2, 127.8, 127.6, 126.1, 125.9, 125.9, 125.8, 94.3 (d, $^1J_{C\text{-}F}$ = 175.8 Hz), 80.8, 40.7 (d, $^2J_{C\text{-}F}$ = 22.7 Hz), 36.1 (d, $^3J_{C\text{-}F}$ = 5.2 Hz), 33.0, 30.7 (d, $J$ = 2.7 Hz), 28.1, 21.4; $^{19}$F NMR $\delta$ −176.8; IR (NaCl) 2980, 2928, 2823, 1724, 1454, 1367, 1150 cm$^{-1}$; MS (ESI+) $m/z$ (%) 503 [M + Na]$^+$ (68), 481 [M + H]$^+$ (83), 425 (100); HRMS $m/z$ calcd for $C_{29}H_{34}O_3FS$ 481.2207, found 481.2218.

**General Methods for Adducts Desulfinylation.** *Raney-Ni:* A solution of the corresponding adducts (0.1 mmol) in THF (0.2 mL) was added over a solution of previously activated Raney-Ni (450 mg) in THF (0.5 mL). The resulting reaction was stirred for 4.5 h at rt, and then the crude was directly filtered on Celite and the pure products were recovered with ether.

*tert-BuLi:* To a solution of the corresponding sulfoxide (0.12 mmol) in dry THF (2 mL) at −78 °C was dropwise added *tert*-BuLi (0.4 mmol, 1.7 M in pentane). When the reaction was complete (30 min), the resulting reaction mixture was hydrolyzed (1 mL of $H_2O$), extracted (3 × 10 mL AcOEt), washed (10 mL of NaCl), dried ($MgSO_4$), and the solvent was removed under reduced pressure.

**(2*R*,3*R*)-3-Fluoro-2,3-diphenylpropyl phenyl sulfone (4a).** Compound **4a** was obtained as a unique diastereomer from sulfone **3a**: yield 84%; colorless oil; $[\alpha]^{20}_D$ 9 ($c$ 1.5, $CHCl_3$); $^1$H NMR $\delta$ 7.80−7.59 (m, 2H), 7.57−7.52 (m, 1H), 7.43−7.38 (m, 2H), 7.22−7.20 (m, 3H), 7.12−7.03 (m, 3H), 6.96−6.93 (m, 2H), 6.83 (d, $J$ = 7.8 Hz, 2H), 5.90 (dd, $^2J_{H\text{-}F}$ = 46.4 and $J$ = 3.2 Hz, 1H), 3.86−3.57 (m, 3H); $^{13}$C NMR $\delta$ 139.5, 137.2, 136.9, 135.4, 133.5, 129.6, 129.2, 129.1, 128.8, 128.3, 128.1, 127.9, 127.5, 127.1, 125.6, 125.5, 94.1 (d, $^1J_{C\text{-}F}$ = 181.1 Hz), 57.7 (d, $^3J_{C\text{-}F}$ = 3.5 Hz), 47.1 (d, $^2J_{C\text{-}F}$ = 22.6 Hz); $^{19}$F NMR $\delta$ −188.8; IR (NaCl) 3026, 2905, 1504, 1304, 1152, 705 cm$^{-1}$; MS (ESI+) $m/z$ (%) 731 [2M + Na]$^+$ (30), 377 [M + Na]$^+$ (12), 193 (100); HRMS $m/z$ calcd for $C_{21}H_{19}O_2FNaS$ 377.0982, found 377.0994.

**(2*R*)-2-[(*R*)-Fluoro(phenyl)methyl]-4-phenylbutyl phenyl sulfone (4k).** Compound **4k** was isolated from the 80:20 diastereoisomeric mixture (**4k** + **4k′**) obtained from **3k** + **3k′**. Chromatography: *n*-hexane/AcOEt, 15:1; yield 65%; colorless oil; $[\alpha]^{20}_D$ 18 ($c$ 1.5, $CHCl_3$); $^1$H NMR $\delta$ 7.92−7.80 (m, 2H), 7.72−7.63 (m, 1H), 7.57 (m, 2H), 7.34−7.29 (m, 3H), 7.23−7.13 (m, 5H), 6.97−6.92 (m, 2H), 5.86 (dd, $^2J_{H\text{-}F}$ = 46.8 and $J$ = 3.6 Hz, 1H), 3.44 (dd, $J$ = 14.5, 7.0 Hz, 1H), 3.12 (dd, $J$ = 14.5, 4.8 Hz, 1H), 2.68−2.33 (m, 2H), 2.47−2.33 (m, 1H), 1.86−1.74 (m, 2H); $^{13}$C NMR $\delta$ 140.8, 139.5, 137.9, 137.6, 133.8, 133.4, 129.4, 129.2, 129.1, 128.5, 128.4, 128.4, 128.3, 128.2, 127.9, 126.0, 125.1, 125.0, 94.32 (d, $^1J_{C\text{-}F}$ = 177.5 Hz), 56.14 (d, $^3J_{C\text{-}F}$ = 3.2 Hz), 39.16 (d, $^2J_{C\text{-}F}$ = 22.1 Hz), 32.79, 29.04 (d, $^3J_{C\text{-}F}$ = 4.4 Hz); $^{19}$F NMR $\delta$ −195.4; IR (NaCl) 3032, 2927, 1448, 1307, 1149, 699 cm$^{-1}$; MS (ESI+) $m/z$ (%) 787 [2M + Na]$^+$ (13), 767 (37), 405 [M + Na]$^+$ (59), 363 [M − F]$^+$ (69), 143 (100); HRMS $m/z$ calcd for $C_{23}H_{23}O_2FNaS$ 405.1295, found 405.1255.

***tert*-Butyl (3*R*,4*R*)-4-Fluoro-4-phenyl-3-(4-methoxyphenyl)-butanoate (13b).** Compound **13b** was obtained as the major diastereomer from the mixture **12b**/**12b′**. Chromatography: *n*-hexane/AcOEt, 20:1; yield 85%; colorless oil; $[\alpha]^{20}_D$ 37 ($c$ 1.5, $CHCl_3$); $^1$H NMR $\delta$ 7.27−7.26 (m, 2H), 7.10−7.05 (m, 2H), 7.00 (d, $J$ = 8.7 Hz, 2H), 6.77 (d, $J$ = 8.2 Hz, 2H), 5.61 (dd, $^2J_{H\text{-}F}$ = 46.6 and $J$ = 5.1 Hz, 1H), 3.76 (s, 3H), 3.58−3.43 (m, 1H), 2.83−2.42 (m, 2H), 1.29

(s, 9H); $^{13}$C NMR $\delta$ 169.9, 157.6, 137.4, 137.1, 129.1, 129.0, 127.1, 127.0, 125.0, 124.9, 112.4, 95.1 (d, $^{1}J_{C\text{-}F}$ = 177.7 Hz), 79.6, 54.1, 46.7 (d, $^{2}J_{C\text{-}F}$ = 23.0 Hz), 36.8 (d, $^{3}J_{C\text{-}F}$ = 4.1 Hz), 26.9; $^{19}$F NMR $\delta$ −183.5; IR (NaCl) 3026, 2994, 2924, 1731, 1152, 702 cm$^{-1}$; MS (ESI+) $m/z$ (%) 367 [M + Na]$^+$ (30), 263 (94), 225 (100); HRMS $m/z$ calcd for $C_{21}H_{25}O_3FNa$ 367.1679, found 367.1696.

***tert*-Butyl (3*R*,4*R*)-4-Fluoro-4-phenyl-3-(4-tolyl)butanoate (13c).** Compound **13c** was obtained as the major diastereomer from the mixture **12c**/**12c′**. Chromatography: *n*-hexane/AcOEt, 20:1; yield 84%; white solid; mp 45−46 °C; $[\alpha]^{20}_D$ 49 (*c* 0.9, $CHCl_3$); $^1$H NMR $\delta$ 7.29−7.26 (m, 2H), 7.13−7.10 (m, 2H), 7.06−6.97 (m, 4H), 5.61 (dd, $^{2}J_{H\text{-}F}$ = 46.6 and *J* = 5.5 Hz, 1H), 3.60−3.45 (m, 1H), 2.72−2.54 (m, 2H), 2.54 (s, 3H), 1.28 (s, 9H); $^{13}$C NMR $\delta$ 170.9, 138.4, 138.1, 136.5, 135.2, 128.8, 128.7, 128.2, 128.1, 126.1, 126.0, 96.2 (d, $^{1}J_{C\text{-}F}$ = 177.6 Hz), 80.6, 48.0 (d, $^{2}J_{C\text{-}F}$ = 23.2 Hz), 37.7 (d, $^{3}J_{C\text{-}F}$ = 4.2 Hz), 27.9, 21.1; $^{19}$F NMR $\delta$ −182.4; IR (KBr) 3026, 2991, 2925, 1731, 1152, 699 cm$^{-1}$; MS (ESI+) $m/z$ (%) 537 (33), 519 (32), 351 [M + Na]$^+$ (72), 253 (100); HRMS $m/z$ calcd for $C_{21}H_{25}O_2FNa$ 351.1730, found 351.1736.

***tert*-Butyl (3*R*,4*R*)-4-Fluoro-3-(4-fluorophenyl)-4-phenylbutanoate (13d).** Compound **13d** was obtained as the major diastereomer from the mixture **12d**/**12d′**. Chromatography: *n*-hexane/AcOEt, 20:1; yield 86%; white solid; mp 82−84 °C; $[\alpha]^{20}_D$ 49 (*c* 1.6, $CHCl_3$); $^1$H NMR $\delta$ 7.34−7.27 (m, 2H), 7.09−7.03 (m, 4H), 6.94−6.89 (m, 2H), 5.64 (dd, $^{2}J_{H\text{-}F}$ = 45.9 Hz and *J* = 1H), 3.61−3.47 (m, 1H), 2.75−2.59 (m, 2H), 1.28 (s, 9H); $^{13}$C NMR $\delta$ 170.7, 161.9 (d, $^{1}J_{C\text{-}F}$ = 245.2 Hz), 138.1, 137.9, 133.8, 129.4 (d, $^{3}J_{C\text{-}F}$ = 8.1 Hz), 128.3, 128.1, 125.8, 125.7, 114.8, (d, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 95.9 (d, $^{1}J_{C\text{-}F}$ = 178.0 Hz), 80.8, 47.9 (d, $^{2}J_{C\text{-}F}$ = 22.9 Hz), 37.8 (d, $^{3}J_{C\text{-}F}$ = 4.1 Hz), 27.9; $^{19}$F NMR $\delta$ −115.8, −185.0; IR (KBr) 3012, 2998, 2920, 1732, 1156, 704 cm$^{-1}$; MS (ESI+) $m/z$ (%) 355 [M + Na]$^+$ (77), 257 (100), 211 (83); HRMS $m/z$ calcd for $C_{20}H_{22}O_2F_2Na$ 355.1480, found 355.1488.

***tert*-Butyl (3*S*)-3-[(*R*)-Fluoro(phenyl)methyl]-5-phenylpentanoate (13k).** Compound **13k** was obtained as the unique diastereomer from ester **12k**: yield 80%; colorless oil; $[\alpha]^{20}_D$ 16 (*c* 2.0, $CHCl_3$); $^1$H NMR $\delta$ 7.30−7.19 (m, 5H), 7.17−7.14 (m, 2H), 7.10−7.08 (m, 2H), 5.56 (dd, $^{2}J_{H\text{-}F}$ = 47.1 and *J* = 4.6 Hz, 1H), 2.75−2.65 (m, 1H), 2.58−2.50 (m, 1H), 2.47−2.39 (m, 2H), 2.30−2.22 (m, 1H), 1.90−1.78 (m, 1H), 1.71−1.61 (m, 1H), 1.46 (s, 9H); $^{13}$C NMR $\delta$ 171.8, 142.0, 138.9, 138.6, 129.3, 128.4, 128.3, 128.3, 128.3, 128.1, 125.8, 125.8, 125.7, 95.9 (d, $^{1}J_{C\text{-}F}$ = 174.7 Hz), 80.7, 40.9 (d, $^{2}J_{C\text{-}F}$ = 22.4 Hz), 36.2 (d, $^{3}J_{C\text{-}F}$ = 4.3 Hz), 33.3, 30.3, 28.1; $^{19}$F NMR $\delta$ −187.8; IR (NaCl) 3020, 2993, 2931, 1727, 1149, 700 cm$^{-1}$; MS (ESI+) $m/z$ (%) 365 [M + Na]$^+$ (15), 249 (20), 189 (80), 129 (100); HRMS $m/z$ calcd for $C_{22}H_{27}O_2FNa$ 365.1887, found 365.1886.

**General Procedure for Synthesis of Compounds 5a−7a (Scheme 4). General Procedure for the Desulfonylation.** The corresponding sulfone (0.1 mmol) was dissolved in 0.4 mL of $CH_2Cl_2$ and added to a solution of magnesium (10 equiv, previously flame-dried under a stream of argon) in 1 mL of MeOH under argon atmosphere. After complete consumption, 10 equiv more of magnesium was added. When the reaction was finished (as monitored by TLC), the crude was directly filtered on silica. The residue was purified by flash column chromatography.

**1,1′-[(1*R*,2*R*)-1-Fluoropropane-1,2-diyl]dibenzene (5a).** Compound **5a** was obtained as the unique diastereomer from sulfone **4a**. Chromatography: *n*-hexane/AcOEt, 10:1; yield 63%; colorless oil; $[\alpha]^{20}_D$ 54 (*c* 0.45, $CHCl_3$); $^1$H NMR $\delta$ 7.35−7.28 (m, 5H), 7.24−7.20 (m, 5H), 5.46 (dd, $^{2}J_{H\text{-}F}$ = 46.5 and *J* = 7.3 Hz, 1H), 3.32−3.71 (m, 1H), 1.20 (d, *J* = 7.2 Hz, 3H); $^{13}$C NMR $\delta$ 142.0, 141.9, 138.8, 138.5, 128.4, 128.3, 128.3, 128.2, 128.1, 126.7, 126.4, 126.4, 98.1, (d, $^{1}J_{C\text{-}F}$ = 176.0 Hz), 46.1 (d, $^{2}J_{C\text{-}F}$ = 23.2 Hz), 17.2 (d, $^{3}J_{C\text{-}F}$ = 5.6 Hz); $^{19}$F NMR $\delta$ −174.2; IR (NaCl) 3029, 2995, 2926, 1452, 1216 cm$^{-1}$; MS (ESI+) $m/z$ (%) 214 [M]$^+$ (10), 194 (23), 179 (81), 105 (100); HRMS $m/z$ calcd for $C_{15}H_{15}F$ 214.1158, found 214.1154.

**General Procedure for Addition and Desulfonylation.** To a solution of sulfone (0.085 mmol, dr >98:2) in THF (2.1 mL), cooled at −78 °C, was added a 2.5 M solution of *n*-BuLi in hexane (1.5 equiv). The resulting solution was maintained for 20 min, and then electrophile (1.5 equiv) was added. The mixture was stirred at −78 °C for 1 h, and then saturated solution $NH_4Cl$ (5 mL) was added. The organic phase was separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The residue was dissolved in 0.4 mL of $CH_2Cl_2$, and then the general procedure for the desulfonylation was followed.

**1,1′-[(1*R*,2*R*)-1-Fluorobutane-1,2-diyl]dibenzene (6a).** Compound **6a** was obtained as the unique diastereomer from sulfone **4a** and MeI. Chromatography: *n*-hexane/AcOEt, 10:1; yield 53%; colorless oil; $[\alpha]^{20}_D$ 64 (*c* 0.85, $CHCl_3$); $^1$H NMR $\delta$ 7.28−7.20 (m, 6H), 7.19−7.11 (m, 4H), 5.47 (dd, $^{1}J_{H\text{-}F}$ = 46.6 and *J* = 6.6 Hz, 1H), 2.90−2.77 (m, 1H), 1.65−1.54 (m, 2H), 0.68 (d, *J* = 7.3 Hz, 3H); $^{13}$C NMR $\delta$ 139.9, 139.8, 139.2, 128.9, 128.9, 128.2, 128.2, 128.1, 128.1, 126.7, 126.3, 126.2, 97.2, (d, $^{1}J_{C\text{-}F}$ = 175.9 Hz), 54.3 (d, $^{2}J_{C\text{-}F}$ = 22.2 Hz), 24.5 (d, $^{3}J_{C\text{-}F}$ = 4.6 Hz), 11.9; $^{19}$F NMR $\delta$ −177.0; IR (NaCl) 3026, 2994, 2930, 1451, 1210 cm$^{-1}$; MS (EI) $m/z$ (%) 228 [M]$^+$ (9), 208 (61), 193 (34), 179 (35), 115 (47), 91 (100); HRMS $m/z$ calcd for $C_{16}H_{17}F$ 228.1314, found 228.1302.

**Methyl (3*R*,4*R*)-4-Fluoro-3,4-diphenylbutanoate (7a).** Compound **7a** was obtained as the unique diastereomer from sulfone **4a** and $ClCO_2Me$. Chromatography: *n*-hexane/AcOEt, 20:1; yield 55%; colorless oil; $[\alpha]^{20}_D$ 55 (*c* 0.3, $CHCl_3$); $^1$H NMR $\delta$ 7.28−7.26 (m, 3H), 7.24−7.15 (m, 3H), 7.15−7.09 (m, 4H), 5.68 (dd, $^{1}J_{H\text{-}F}$ = 46.5 and *J* = 5.4 Hz, 1H), 3.71−3.60 (m, 1H), 3.56 (s, 3H), 2.89−2.69 (m, 2H); $^{13}$C NMR $\delta$ 172.1, 138.1, 138.1, 137.8, 128.8, 128.3, 128.2, 128.1, 127.1, 126.0, 125.9, 95.9 (d, $^{1}J_{C\text{-}F}$ = 178.0 Hz), 51.7, 48.1 (d, $^{2}J_{C\text{-}F}$ = 23.0 Hz), 36.3 (d, $^{3}J_{C\text{-}F}$ = 4.7 Hz); $^{19}$F NMR $\delta$ −183.3; IR (NaCl) 3023, 2990, 2929, 1735, 1140, 695 cm$^{-1}$; MS (EI) $m/z$ (%) 295 [M + Na]$^+$ (35), 253 [M − F]$^+$ (18), 221 (31), 193 (100); HRMS $m/z$ calcd for $C_{17}H_{17}O_2FNa$ 295.1104, found 295.1113.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

$^1$H and $^{13}$C NMR for compounds **3a−e**, **3h**, **3j**, **3k**, **3l** + **3l′**, **12a**, **12e**, **12f**, **12i**, **12k**, **12j**, **4a**, **4k**, **13b−d**, **13k**,(**5−7**)**a**, and X-ray ORTEP and crystallographic data for compound **3e** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

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## ■ DEDICATION

Dedicated to the late Prof. Dr. Guy Solladié for his valuable contribution to asymmetric organic synthesis mediated by the sulfinyl group.

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(28) Reaction with chalcone (2 equiv) as the Michael acceptor, in THF at −78 °C, afforded a 2:1 mixture of 1,2 and 1,4-adducts, both being obtained as a 60:40 diastereoisomeric mixture.

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